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MULTIPLE MYELOMA

A Review of Eighty-Three Proved Cases

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One hundred years ago, in November 1845, Sir James Watson sent a test tube of urine obtained from a 45 year old tradesman to Dr. Henry Bence-Jones with an accompanying note inquiring as to the nature of a strange substance present in that urine. This substance, then called "animal matter," has since become known as Bence-Jones protein.[1] MacIntyre[2] reported this case in 1850 in the *Medico-Chirurgical Transactions*.

Dalrymple[3] examined and described pathologically two ribs of an affected patient and reported the condition as mollities ossium in 1846. However, von Rustizky[4] is said to have been the first to describe the condition under the title "multiples myelom" in 1873, and Kahler[5] is credited with having associated this disease with the occurrence of Bence-Jones protein in the urine.

Since these early reports additions have been made to the literature steadily and at a somewhat increasing rate as the facilities for diagnosis and a greater knowledge of the unusual manifestations of this affliction have become more widespread. The most signal effort to systematize the present knowledge of this disease was that of Geschickter and Copeland[6] in 1928, when they reviewed all of the cases of proved multiple myeloma appearing in the literature up to that time and added 13 of their own to bring the total up to 425.

This present study deals with 83 cases of multiple myeloma in which the diagnosis has been verified by examination of pathologic material. The study includes all such cases seen at the Mayo Clinic through December 1945. Forty-nine cases were confirmed by means of sternal aspiration, 26 by biopsy and 8 by necropsy. Ten patients who had apparently solitary intramedullary tumors (not included in the 83 cases mentioned) were also seen, and the condition was verified by biopsy. These will be considered separately, not as indubitable instances of solitary myeloma, but as too uncertain of being multiple to be included in the general series. Eleven additional cases of extramedullary, oronasal myeloma were also noted, but with the exception of 1 case in which the myelomas later became multiple these will not be included, as they have been fully reported elsewhere.[7]

When this subject was last reported on from the clinic,[8] 32 cases of pathologically confirmed multiple myeloma had been observed. The present group of cases was drawn from more than 350 in which a diagnosis of multiple myeloma had been made on clinical grounds. In many of these, the evidence was almost indisputable but, unfortunately, pathologic material was lacking. Because of newer improvements in technic, most of the cases of proved multiple myeloma have been recent ones. Eighteen were seen in one period of six months during 1945.

CLINICAL MANIFESTATIONS

Pain.—All investigators to whose works we have had reference have observed that pain was the outstanding feature and frequently the sole symptom of which patients who had this disease complained. In this study it was present in 86 per cent of cases (fig. 3) at the time of first admission of the patients, which makes it the most constant finding by far. The two regions most often involved were the thorax and the lumbar spinal segment. Its onset frequently dated from some strain or slight trauma such as "the time I bumped my chest on the corner of the desk" or from "last January when I strained my back shoveling snow."

This pain was found as a rule to be steadily progressive, though with daily and weekly variations, only occasionally undergoing any prolonged remission which would have brought it into accord with Geschickter and Copeland's pain cycle.[6] Batts[9] was likewise unable to fit the majority of his patients into such a pattern.

On the few occasions when a remission did follow the initial onset of pain the pain usually was induced subsequent to trauma.

The pain that these patients experienced was almost always aggravated by exertion, coughing and sneezing and eased by rest. Many patients said that if they did not move they felt all right. Pain in the night was not common, contrasting with other malignant states.

Associated with this pain there was occasionally noted a striking, exquisite, yet superficial tenderness. The lightest palpation over the involved regions was sufficient to elicit an immediate and extremely sharp response from the patient. This tenderness was not found to be due to pathologic fractures, but local fragility of bone may have been a factor.

From the Division of Medicine, Mayo Clinic.

1. Jones, H. B.: On a New Substance Occurring in the Urine of a Patient with Mollities Ossium, Phil. Tr., London **138**: 55-62, 1848.
2. MacIntyre, W.: Case of Mollities and Fragilitas Ossium, Accompanied with Urine Strongly Charged with Animal Matter, Med.-Chir. Tr., London **33**: 211-232, 1850.
3. Dalrymple, J.: On the Microscopic Character of Mollities Ossium, Dublin J. M. Sc. **2**: 85-95, 1846.
4. von Rustizky, J.: Multiples Myelom, Deutsche Ztschr. f. Chir. **3**: 162-172, 1873.
5. Kahler, O.: Zur Symptomatologie des multiplen Myeloms: Beobachtung von Albumosurie, Prag. med. Wchnschr. **14**: 33-45, 1889.
6. Geschickter, C. F., and Copeland, M. M.: Multiple Myeloma, Arch. Surg. **16**: 807-863 (April) 1928.
7. Figi, F. A.; Broders, A. C., and Havens, F. Z.: Plasma Cell Tumors of the Upper Part of the Respiratory Tract, Ann. Otol., Rhin. & Laryng. **54**: 283-297 (June) 1945.
8. (*a*) Ghormley, R. K., and Pollock, G. A.: Multiple Myeloma, Surg., Gynec. & Obst. **69**: 648-655 (Nov.) 1939. (*b*) Ghormley, R. K.; Pollock, G. A.; Hall, B. E., and Beizer, L. H.: Multiple Myeloma, Surg., Gynec. & Obst. **74**: 242-244 (Feb.) 1942.
9. Batts, M., Jr.: Multiple Myeloma: Review of Forty Cases, Arch. Surg. **39**: 807-823 (Nov.) 1939.

The characteristics of this pain alone, its location and progression and the rest, ease and freedom enjoyed by the patient at night, actually suggested the proper diagnosis to us clinically on one occasion. However, as a rule the clinical findings are entirely nonspecific.

Fig. 1.—Smear of sternal marrow from same patient as in figure 4. Note contrast between the case illustrated in figures 1 and 4 and the case illustrated in figures 2 and 5. In the former case there were extreme destructive changes in the skeleton but the bone marrow showed much less change from normal than in figure 2; in the latter case the skeleton did not reveal any gross abnormalities but the bone marrow was characteristic of extremely malignant multiple myeloma.

Fig. 2.—Smear of sternal marrow from same patient as in figure 5. The bone marrow was characteristic of extremely malignant multiple myeloma.

In 10 per cent of instances the pain had a rootlike distribution, often sciatic, and was usually found to be associated with compression of one or more vertebrae.

Fracture.—Pathologic fracture was encountered in a surprisingly small number of these cases (16 per cent), although occasionally evidence of old fracture of the ribs was present on roentgenologic examination of the thorax. When it was observed, the fracture usually involved the proximal third of the femur or the ribs, which is to be expected, since the disease primarily is one of the red bone marrow. These figures do not include compression, or "compression fractures" of the vertebrae.

Neurologic Manifestations.—Neurologic manifestations, such as root pain, as mentioned previously, and paraplegia, often a rather early development, were encountered in 12 cases (14 per cent). Once paralysis intervened, the outlook was definitely poor, although one of our patients lived for seven and a half years following laminectomy after the onset of paraplegia.

Bleeding.—Several writers have mentioned abnormal bleeding,[10] largely from the nose and gums. It is not as a rule associated with any defect in the clotting factors, except possibly of clot retraction. It is, however, almost invariably accompanied with a high concentration of serum globulin.[10h] In Schumacher's case the concentration of protein was 23.27 Gm. in 100 cc. of serum, and that of globulin was 16.02 Gm. Abnormal bleeding was observed in 6 instances in our series, and in 2 it was a distressing and most troublesome symptom, so much so that 1 of these patients received radium therapy locally in an endeavor to stop it. In all these cases the serum protein and serum globulin were appreciably increased, the lowest being 8.1 Gm. of protein in 100 cc. of serum and the highest, 14.1

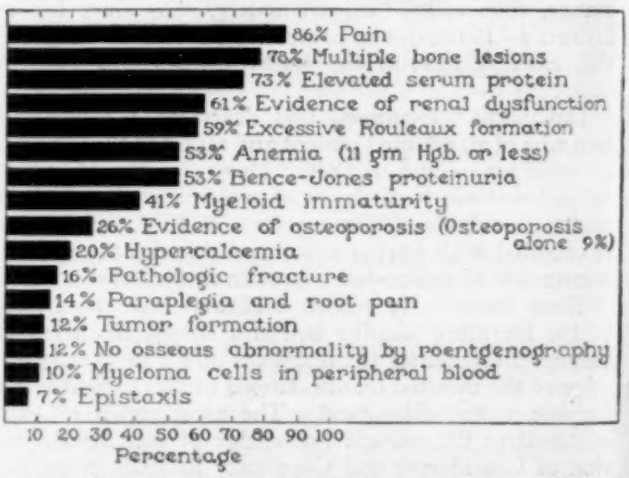
86% Pain
78% Multiple bone lesions
73% Elevated serum protein
61% Evidence of renal dysfunction
59% Excessive Rouleaux formation
53% Anemia (11 gm. Hgb. or less)
53% Bence-Jones proteinuria
41% Myeloid immaturity
26% Evidence of osteoporosis (Osteoporosis alone 9%)
20% Hypercalcemia
16% Pathologic fracture
14% Paraplegia and root pain
12% Tumor formation
12% No osseous abnormality by roentgenography
10% Myeloma cells in peripheral blood
7% Epistaxis
10 20 30 40 50 60 70 80 90 100
Percentage

Fig. 3.—Percentage of occurrence of clinical and laboratory abnormalities in 83 cases of proved multiple myeloma.

10. (*a*) Foord, A. G.: Hyperproteinemia, Autohemagglutination and Renal Insufficiency and Abnormal Bleeding in Multiple Myeloma, Ann. Int. Med. **8**: 1071-1089 (March) 1935. (*b*) Jackson, H., Jr.; Parker, F., Jr., and Bethea, J. M.: Studies of Diseases of the Lymphoid and Myeloid Tissues: Plasmatocytomata and Their Relation to Multiple Myelomata, Am. J. M. Sc. **181**: 169-180 (Feb.) 1931. (*c*) Osgood, E. E., and Hunter, W. C.: Plasma Cell Leukemia, Folia haemat. **52**: 369-383 (Nov.) 1934. (*d*) Patek, A. J., Jr., and Castle, W. B.: Plasma Cell Leukemia: Consideration of Literature with Report of Case, Am. J. M. Sc. **191**: 788-793 (June) 1936. (*e*) Hertzog, A. J., and Schleicher, E.: Multiple Myeloma: Report of Three Cases, Minnesota Med. **27**: 1011-1013 (Dec.) 1944. (*f*) Schumacher, I. C.; Williams, O. O., and Coltrin, G. S.: Plasma Cell Myeloma and Hyperproteinemia, California & West. Med. **47**: 174-177 (Sept.) 1937. (*g*) Ulrich, H.: Multiple Myeloma, Arch. Int. Med. **64**: 994-1016 (Nov.) 1939. (*h*) Ross, J. P.; Discombe, G., and Robb-Smith, A. H. T.: A Case of Multiple Myelomatosis, with Notes on the Value of Biochemistry in the Diagnosis of Bone Disease, St. Barth. Hosp. Rep. **70**: 221-246, 1937. (*i*) Foord, A. G., and Randall, L.: Hyperproteinemia, Autohemagglutination and Renal Insufficiency in Multiple Myeloma, Am. J. Clin. Path. **5**: 532-547 (Nov.) 1935.

Gm. No correlation with Bence-Jones protein could be obtained, however, as in 2 of the 5 cases the reaction for Bence-Jones protein was negative.

Formation of Tumor.—Formation of tumor was noted rather infrequently as compared to Batts's series, being found in only 10 cases, with a distribution as follows: clavicle, 3; skull, 2; humerus, 1; ribs, 2; sacrum, 1, and sternum, 1.

Pulmonary and Gastrointestinal Symptoms.—Pulmonary and gastrointestinal symptoms were no more frequent than one might have expected in a group of debilitated persons in this age range, and we were unable to develop any pattern of association such as suggested by previous authors.[6]

In 82 of the cases reported, roentgenograms were available. In 64 of these (78 per cent) multiple lesions were demonstrated. The whole skeleton was seldom roentgenographed, so that an attempt to indicate the relative frequency with which various regions were involved would be subject to obvious error. However, among 64 patients for whom multiple lesions were demonstrated on roentgenography, 58 had roentgenograms of the skull, of which 72 per cent were positive; 53 had roentgenograms of the thorax, 70 per cent of which showed such changes, and 51 had roentgenograms of the spinal column, 53 per cent of which showed the same discrete osteolytic regions.

As stated previously, pathologic fractures were noted in only 16 per cent of the patients in this series.

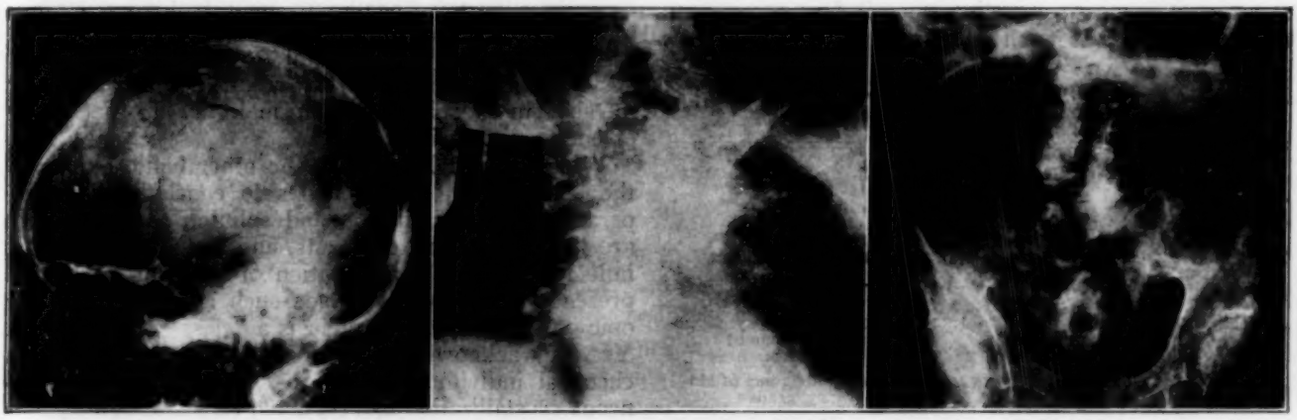

Fig. 4.—Extreme destructive changes in the skeleton of a patient who had multiple myeloma.

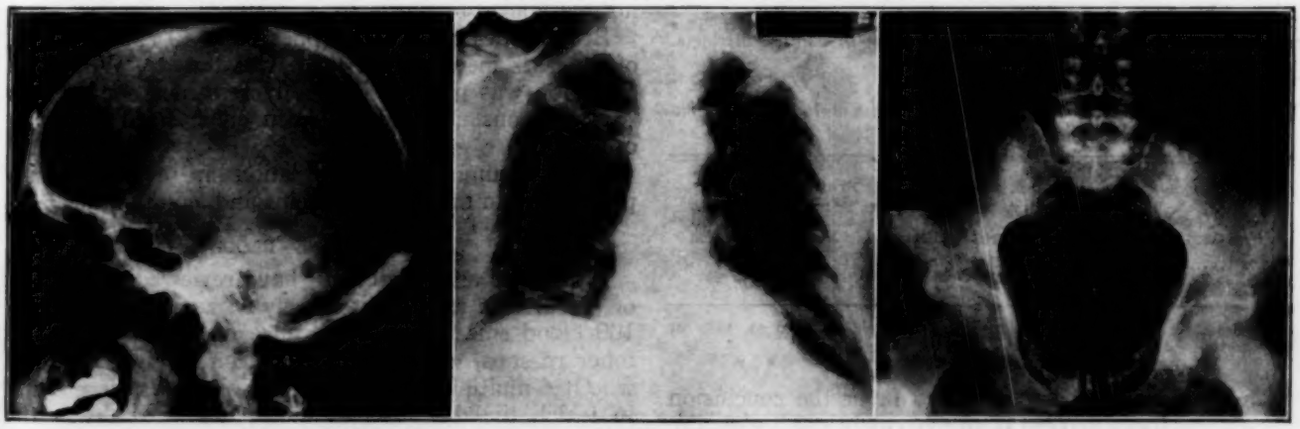

Fig. 5.—Skeleton of a patient who had multiple myeloma. There are no gross abnormalities.

Age and Sex.—The average and median ages of these persons were virtually the same, approximately 57 years, which agrees closely with the reports of others.[11] There was an age span of 20 years on either side. The eldest was 78 and the youngest was 37 years of age. Men outnumbered women by about 3 to 1: men 76 per cent, women 24 per cent.

ROENTGENOGRAPHIC CHANGES

Discrete osteolytic regions in the skeleton of an adult man, especially when multiple, are almost always presumptive evidence of multiple myeloma. This is the so-called classical picture produced in the bones by this disease as it appears in the roentgenogram (figs. 1 and 4). When it occurs, it should be substantiated by further appropriate diagnostic measures.

Other changes which occur with appreciable regularity are chiefly noted in the spinal column and include osteoporosis, compression of the vertebral bodies and ballooning of the intervertebral disks. These changes in themselves, of course, are not nearly so suggestive of multiple myeloma as the punched-out, osteolytic lesions, but in conjunction with an excessively high erythrocyte sedimentation rate, for example, their significance is notably enhanced.

These changes, usually found together, were noted in 21 cases, or 26 per cent of the whole group for which roentgenograms were available. In 7 cases (9 per cent) they constituted the only changes seen.

In 12 per cent of these cases, in the majority of which the serum proteins were elevated and inversion of the albumin-globulin ratio, excessive formation of rouleaux in smears of the peripheral blood and Bence-Jones proteinuria were present, no abnormalities of the osseous system whatsoever (figs. 2 and 5) were demonstrated

11. (*a*) Geschickter and Copeland.[9] (*b*) Ross, Discombe and Robb-Smith.[10a] (*c*) Piney, A., and Riach, J. S.: Multiple Myeloma: Aleukaemic and Leukaemic. Folia haemat. **46**: 37-55, 1931.

by roentgenography (all roentgenograms included head, thorax and spinal column, and two thirds were complete). It should therefore be clear that multiple myeloma is not limited to those cases in which gross bony changes develop, and the diagnosis must in no instance be prejudiced by the absence of these changes.

BENCE-JONES PROTEIN

Historically, Bence-Jones protein is the most significant of the clinical laboratory findings in cases of this disease, even though it is now known to be found in other conditions and is observed in only somewhat more than half of the cases of proved multiple myeloma. Perhaps this figure will drop even lower as clinical appreciation of this disease is otherwise stimulated. However, it is most suggestive when it does occur, and has been the focus of much interest.

TABLE 1.—*Cases in Which Bence-Jones Protein Was Present Not Associated with Multiple Myeloma*

Case	Sex	Age, Yrs.	Roentgenographic Changes	Protein, Gm. in Each 100 Cc. of Serum	Albumin-Globulin Ratio	Sedimentation Rate, Mm. in 1 Hr.	Diagnosis
1	M	32	In spine, femur	...	.....	...	Chronic lymphatic leukemia
2	M	69	In skull	9.8	1:3.1	161	At necropsy: adenocarcinoma of stomach
3	F	63	None	8.2	1:1.5	106	Carcinoma of kidney, grade 4
4*	M	50	.....	...	.....	...	Inactive pulmonary tuberculosis; prostatitis

* In case 4 Bence-Jones protein was present in 1930 and in 1939. This patient was living in 1941. There was no evidence of multiple myeloma.

TABLE 2.—*Relation of Bence-Jones Proteinuria to Albuminuria and Serum Proteins*

Bence-Jones Proteinuria	Albuminuria		Serum Protein		Total Cases
	Absent	Present *	Elevated	Low or Normal	
Present.....	8	32	18	9	40
Absent.....	23	13	16	2	36

* Albuminuria, grade 2 or more (on the basis of 1 to 4), with or without casts and red blood cells.

The evidence at hand seems to favor the conclusion that Bence-Jones protein is an extremely small globulin, or group of small globulins, with a molecular weight of approximately 30,000. Its small size may well account for its frequent occurrence in the urine as contrasted with the rarity with which it has been noted in the blood.

Coley [12] found Bence-Jones protein in "about 8 per cent of all cases." His personal series included 16 cases. Batts [9] found it in 50 per cent; Ghormley and Pollock,[8a] reporting from the Mayo Clinic in 1939, found it in 35 per cent of proved cases, 51 per cent of their whole series. Geschickter and Copeland [6] in their review of 425 proved cases, including 13 of their own, noted an incidence of 65 per cent.

Bence-Jones protein has been reported [13] as occurring in the following conditions other than multiple myeloma: metastatic carcinoma of the bone, multiple sarcoma of the bone, senile osteomalacia, fibrocystic disease, comminuted fracture, tumor of the jaws, lymphatic leukemia, myelogenous leukemia and polycythemia. We have encountered it, unassociated with multiple myeloma, in the instances shown in table 1.

The nature of Bence-Jones protein and its mode and site of production have been the source of much speculation and investigation.

In a most extensive work on the subject Hopkins and Savory,[14] in 1911, found that Bence-Jones protein contains all the amino acids characteristic of a typical protein and is characterized by a high proportion of the aromatic groupings. They found it to have less power as an antigen than serum proteins and to contain less histidine than did globin. In their opinion it seemed to stand alone in respect to its chemical composition as well as its physicochemical properties. They suggested that it might be the result of an incomplete metabolism as well as an abnormal one, but that it was of endogenous origin.

Wintrobe and Buell,[15] on the other hand, expressed the belief that it is erroneous to conclude that temperatures of precipitation and solution of the protein are physicochemical constants, and stated that they are influenced by the concentration of the protein, p_H and presence of other compounds such as urea. In their opinion, Bence-Jones protein is a "class" of substances. Yet they acknowledged that it had been isolated as a chemical individual in certain cases in which spontaneous crystallization had occurred on standing.

Bayne-Jones and Wilson [16] found Bence-Jones protein to be immunologically distinct from proteins of normal human serum.

Bence-Jones proteinuria appeared in 40 (53 per cent) of 76 cases in which the urine was tested. When this condition was present, it usually remained so, but this was not constant, and has been emphasized by many others.

Table 2 summarizes the relationship of Bence-Jones proteinuria to the serum proteins and albuminuria.

PERIPHERAL BLOOD

Morissette and Watkins [17] have reviewed this aspect of the disease rather extensively in an investigation of 100 blood smears which, because of "greasiness" [18] or other reasons, were suspected of coming from patients who had multiple myeloma. Fifty-six cases were found in which the diagnosis of multiple myeloma was the most acceptable from clinical and laboratory studies (in only 19 of these was the diagnosis pathologically confirmed). The significant hematologic findings in these 56 were (1) anemia, (2) excessive formation of rouleaux, (3) immaturity of both erythrocytes and leukocytes, (4) lymphocytosis, (5) eosinophilia and (6) presence of myeloma cells and atypical plasma cells.

Anemia.—Anemia has been repeatedly noted as one of the important, frequently occurring features of mul-

12. Coley, W. B.: Multiple Myeloma, Ann. Surg. **93**: 77-89 (Jan.) 1931.

13. (*a*) Geschickter and Copeland.[6] (*b*) Ross, Discombe and Robb-Smith.[10a] (*c*) Boggs, T. R., and Guthrie, C. G.: The Bence-Jones Proteinuria in Conditions Other than Myelomatosis: An Instance Associated with Metastatic Carcinoma, Bull. Johns Hopkins Hosp. **23**: 353-356 (Dec.) 1912.

14. Hopkins, F. G., and Savory, H.: A Study of Bence-Jones Protein and of the Metabolism in Three Cases of Bence-Jones Proteinuria, J. Physiol. **42**: 189-250 (March) 1911.

15. Wintrobe, M. M., and Buell, M. V.: Hyperproteinemia Associated with Multiple Myeloma, with Report of Case in Which Extraordinary Hyperproteinemia Was Associated with Thrombosis of Retinal Veins and Symptoms Suggesting Raynaud's Disease, Bull. Johns Hopkins Hosp. **52**: 156-165 (Feb.) 1933.

16. Bayne-Jones, S., and Wilson, D. W.: Immunological Reactions of Bence-Jones Proteins: I. Differences Between Bence-Jones Proteins and Human Serum Proteins, Bull. Johns Hopkins Hosp. **33**: 37-43 (Feb.) 1922.

17. Morissette, L., and Watkins, C. H.: Multiple Myeloma: Diagnostic Value of the Blood Smear, Proc. Staff Meet., Mayo Clin. **17**: 433-440 (July) 1942.

18. A smear of the peripheral blood was referred to as "greasy" if it appeared as though it had been made on a dirty or an oily slide.

tiple myeloma and has been ascribed to (1) bone marrow replacement, (2) toxic inhibition and (3) renal failure. None of these has been an entirely satisfactory explanation. But in any event the response to the usual therapeutic measures is generally disappointing.

In this group anemia was common, 53 per cent of the patients having hemoglobin values, by the photelometer method, of less than 11 Gm. per hundred cubic centimeters of blood. Fifty-six per cent of the patients had an erythrocyte count of less than 4,000,000 per cubic millimeter of blood, and 25 per cent had an erythrocyte count of less than 3,000,000 per cubic millimeter. It will be noted, however, that the counts alone are as a rule worth little except as unexplained anemia may provoke further study.

Excessive Formation of Rouleaux.—Excessive formation of rouleaux in cases of multiple myeloma was first stressed by Reimann,[19] although he cited Hewson as having commented on abnormal formation of rouleaux in 1797. Many others have noted it since.

Considered as causes of this phenomenon are slow drying, presence of a hydrophilic colloid (acacia) and increased globulin with a reversal of the albumin-globulin ratio.

Frequently associated with formation of rouleaux is autohemagglutination,[20] which may appear in the red cell counting chamber, is associated with an elevated erythrocyte sedimentation rate and may make cross matching or typing impossible. Snapper[21] suggested carrying on this reaction in an incubator at 28 C. to overcome this tendency.

Excessive formation of rouleaux was noted in 38 of 63 cases (60 per cent) in which examinations of the peripheral blood were made. An extremely close correlation with increased serum globulin and an elevated erythrocyte sedimentation rate was noted. In no instance was increased formation of rouleaux noted in the presence of normal serum globulins, or normal serum protein levels, although it was not mentioned in 4 cases in which the proteins were elevated.

A corollary to formation of rouleaux is an elevation of the erythrocyte sedimentation rate to surprising heights. Our highest uncorrected rate was 176 mm. in one hour by the method of Westergren.

In 45 cases determinations of both the total serum protein and the erythrocyte sedimentation rate were made. In 36 of these there was an increased serum protein (more than 8.0 Gm. per hundred cubic centimeters), and in all but 1 there was a notably increased sedimentation rate, of 100 mm. or more in an hour (Westergren method, not corrected). In that 1 case the serum protein was 10.2 Gm. per hundred cubic centimeters, the albumin-globulin ratio 1:1.6 and the erythrocyte sedimentation rate 35. Of the 9 cases in which the serum protein was normal, in all but 2 there was an erythrocyte sedimentation rate of less than 58 mm. in an hour, and in only 3 of those did it exceed 28 mm. in an hour. Of the 2 mentioned, in 1 there was a sedimentation rate of 107 mm., with a serum protein of 7.8 Gm. per hundred cubic centimeters and an albumin-globulin ratio of 1.5:1.0, and in the other there was a sedimentation rate of 72 mm., with a serum protein of 6.5 Gm. and an albumin-globulin ratio of 3.5:1.0.

Leukocyte Count.—The leukocyte count is usually normal or somewhat low. In 80 per cent of our series it was less than 10,000 per cubic millimeter of blood, and in a third of the 80 per cent it was less than 5,000. However, a leukemoid reaction is fairly common, and on occasions it may be extreme, leading to rather high counts. Barr[22] reported a case in which there was a leukocyte count of 21,000. In Rosenthal and Vogel's[23] case (number 13) the leukocyte count was 48,000. Foord and Randall[10i] reported a case proved by necropsy (number 1) in which there was 18.37 Gm. of protein per hundred cubic centimeters and the leukocyte count was 131,000 terminally with 2 per cent leukoblasts and stem cells, 12 per cent myelocytes and 31 per cent eosinophils.

Morissette and Watkins[17] noted that eosinophilia was occasionally encountered in cases of multiple myeloma, as was lymphocytosis. In this series, however, only 1 case was noted in which significant eosinophilia had been recorded. Leukocytes numbered 6,800 in each cubic millimeter of blood, and 45 per cent of them were eosinophils. Lymphocytosis in these cases was never more than moderate and by no means constant.

Myeloid Immaturity.—Myeloid immaturity as far back as the stem cell was observed with notable frequency. In 41 per cent of 63 cases in which smears of the peripheral blood were submitted for study there was myeloid immaturity to the myelocyte at least. In 20 per cent stem cells were also seen.

Myeloma Cells.—Since Foa,[24] in 1904, and Schridde, who first observed myeloma cells or atypical plasma cells in a case of Aschoff's[25] in 1906, many observers[26] have described them in the peripheral blood stream in cases of multiple myeloma (fig. 6). This may reach the extreme that it did in 1934 in the case of a 49 year old man in which Osgood and Hunter[10c] found 45 to 54 per cent of "plasma cells." This man's spleen was palpable, and he had a leukocyte count ranging from 15,700 to 34,050 per cubic millimeter of blood. His serum protein was elevated to 8.79 Gm. per hundred cubic centimeters, and his albumin-globulin ratio was materially reversed. He had an erythrocyte sedimentation rate of 95 mm. in fifteen minutes, but had no Bence-Jones proteinuria, and only finely granular regions of decalcification in his skull were observed by roentgenologic examination. At necropsy the plasma cells made up 50 per cent of the cellular elements of the bone marrow and showed prominent nucleoli.

Osgood and Hunter considered this to be a true instance of plasma cell leukemia and not multiple myeloma with myeloma cells in the peripheral blood. They held splenomegaly, epistaxis, bleeding from the

19. Reimann, H. A.: Hyperproteinemia as a Cause of Autohemagglutination: Observations in a Case of Myeloma, J. A. M. A. **99**: 1411-1414 (Oct. 22) 1932.

20. (*a*) Ghormley, Pollock, Hall and Beizer.[8b] (*b*) Morissette and Watkins.[17] (*c*) Reimann.[19] (*d*) Stewart, A., and Weber, F. P.: Myelomatosis, Quart. J. Med. **7**: 211-227 (April) 1938. (*e*) Beizer, L. H.; Hall, B. E., and Giffin, H. Z.: The Diagnosis of Multiple Myeloma by Sternal Aspiration, Am. J. M. Sc. **203**: 829-836 (June) 1942.

21. Snapper, I.: Medical Clinics on Bone Diseases: A Text and Atlas, New York, Interscience Publishers, Inc., 1943, pp. 181-211.

22. Barr, D. P.: Multiple Myeloma, Ann. Int. Med. **1**: 884-889 (May) 1928.

23. Rosenthal, N., and Vogel, P.: Value of the Sternal Puncture in the Diagnosis of Multiple Myeloma, J. Mt. Sinai Hosp. **4**: 1001-1019 (March-April) 1938.

24. Foa, P., cited by Meyer, Halpern and Ogden.[2b]

25. Aschoff, L.: Ein Fall von Myeloma, München. med. Wchnschr. **53**: 337, 1906.

26. (*a*) Jackson, Parker and Bethea.[10b] (*b*) Osgood and Hunter.[10c] (*c*) Piney and Riach.[11c] (*d*) Beck, H. G., and McCleary, S.: Multiple Myeloma with Bone Marrow Plasma Cells in the Blood: Report of Case, J. A. M. A. **72**: 480-482 (Feb. 15) 1919. (*e*) Multiple Myeloma, Cabot Case 21012, New England J. Med. **212**: 28-30 (Jan. 3) 1935. (*f*) Piney, A.: Plasma Cell Leukemia, Folia haemat. **30**: 174-182 (Aug.) 1924. (*g*) Ghon, A., and Roman, B.: Ueber pseudoleukämische und leukämische Plasmazellen-Hyperplasie, Folia haemat. **15**: 72-122, 1913. (*h*) Muller, G. L., and McNaughton, E.: Multiple Myeloma (Plasmatocytomata) with Blood Picture of Plasma Cell Leukemia: Report of Two Cases, Folia haemat. **46**: 17-25 (Dec.) 1931. (*i*) Morissette and Watkins.[17]

gums and the clinical course which this patient pursued to be of the type characteristic of leukemia. As further evidence they cited the lack of Bence-Jones proteinuria, of "typical" defects of the bone in the roentgenograms, bone pain and bone fragility. Others have felt that this is a distinction of degree only, not of kind. With this we would concur.

Significant splenomegaly has been noted in cases of typical multiple myeloma,[27] as has hemorrhage, and it should be apparent from the cases reported herein as well as from the reports of others that the absence of Bence-Jones proteinuria and of findings referable to the osseous system is far from conclusive.

Moreover, Osgood and Hunter themselves took note of the transitional cases between their own and the usual multiple myeloma with myeloma cells in the peripheral blood.

In 1937 Reiter and Freeman [28] reported the case of a woman, 66 years of age, in which there were 72 to 74 per cent of plasma cells in the hepatic and pancreatic vessels at necropsy. During life the patient had manifested weakness, had been treated for pernicious anemia and had not had any roentgenographic studies of her skeleton.

Recently Meyer, Halpern and Ogden [29] reviewed all the known cases of multiple myeloma in which there were plasma cells in the peripheral blood and all the purported cases of plasma cell leukemia, of which they listed 4. In a careful consideration of these cases they expressed doubt that any were actually cases of true plasma cell leukemia. They rejected these cases largely on the ground that the absence of osseous lesions had not been adequately established.

They then presented data on a case of their own of "acute plasma cell leukemia" with hemorrhage and purpura, the patient being a 67 year old woman. There were 11,000 to 31,000 leukocytes per cubic millimeter of blood containing up to 44 per cent "plasma cells," 11 Gm. of total serum protein per hundred cubic centimeters and an inverted albumin-globulin ratio. There was no Bence-Jones proteinuria, and the "complete" skeletal roentgenograms demonstrated "no abnormal bone changes." The spleen, liver, lymph nodes and bone marrow were found to be extensively involved at necropsy. Here stress was laid on the absence of tumors of the bone and Bence-Jones proteins as being evidence against multiple myeloma, whereas the bleeding, the visceral involvement and the clinical course were noted as being characteristic of leukemia. The elevated serum protein was discounted as not diagnostic of multiple myeloma.

Because of this Meyer, Halpern and Ogden expressed the belief that their case justified the designation of acute plasma cell leukemia, although they considered it to "complete the chain in the analogy to lymphoid tumors" such as lymphoma and lymphatic leukemia.

However, since we know that otherwise typical multiple myelomas may occur without discrete bony lesions, without Bence-Jones proteinuria, or with splenic and nodal involvement,[30] with bleeding and purpura and with a high percentage of plasma or myeloma cells in the peripheral blood, we cannot feel that this case represents anything other than the leukemic phase of multiple myeloma. It is not clear that any useful purpose is served by creating the impression that "plasma cell leukemia" is a separate entity.

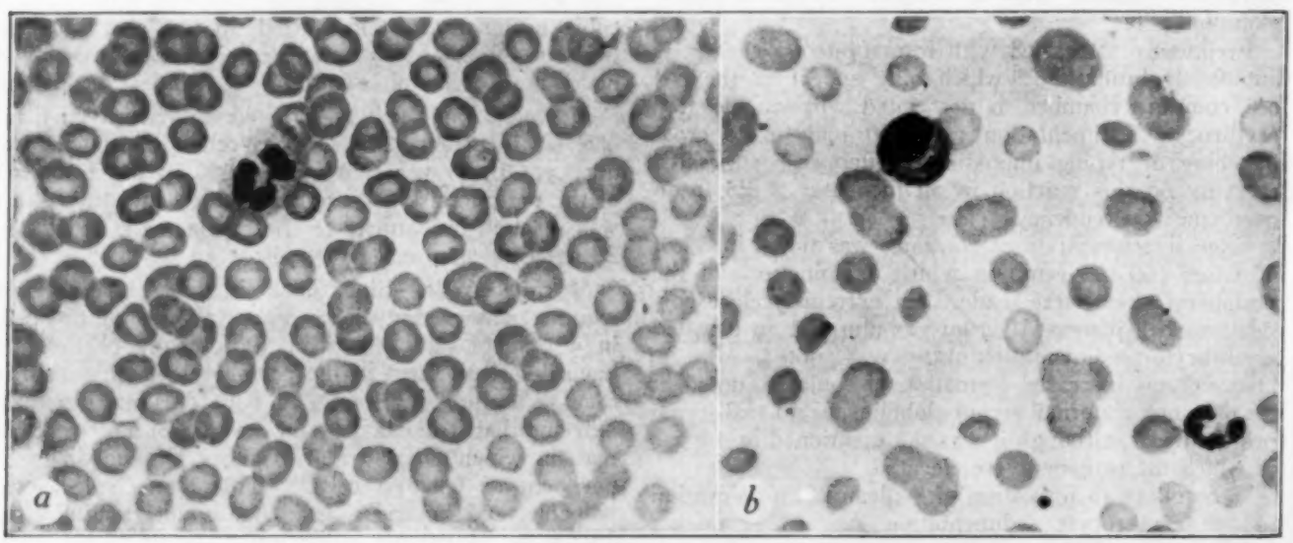

Fig. 6.—Smears of the peripheral blood. (*a*) Normal blood; (*b*) blood in a case of multiple myeloma exhibiting excessive formation of rouleaux and a myeloma cell (upper left).

Morissette and Watkins found atypical plasma cells and myeloma cells in 41 of the 56 cases of multiple myeloma which they studied (73 per cent). In the present series no special effort was made to review the blood smears for myeloma cells. As they were reported by the initial examiner they occurred in only 10 per cent of cases.

One of these patients had 7.5 per cent myeloma cells in his peripheral blood, and another (to be reported on in greater detail separately) with the clinical picture of leukemia had 41.5 to 48 per cent myeloma cells in his peripheral blood.

Of the other observations on the peripheral blood one has been mentioned in connection with the bleeding tendency that some of these patients have, namely, poor clot retraction. This has been observed occasionally among the patients of the present study.

27. Lowenhaupt, E.: Proliferative Lesions in Multiple Myeloma with Special Reference to Those of the Spleen, Am. J. Path. **21**: 171-185 (Jan.) 1945.

28. Reiter, B. R., and Freeman, J. T.: Plasma Cell Leukemia, Am. J. M. Sc. **193**: 38-42 (Jan.) 1937.

29. Meyer, L. M.; Halpern, J., and Ogden, F. N.: Acute Plasma Cell Leukemia, Ann. Int. Med. **22**: 585-598 (April) 1945.

30. Ghormley and Pollock.[6a] Jackson, Parker and Bethea.[10b] Barr.[22] Lowenhaupt.[27]

Rosenthal and Vogel [28] noted thrombopenia in 5 of their 13 cases. We have not observed it with any appreciable frequency, but it should be looked for.

It is also of interest to note that on one, two or three occasions a robin's egg blue background has been observed in the blood smear when stained by the usual method with Wright's stain. These have all been associated with unusually high globulins, but the blue background and the concentration of globulins do not appear to bear a strictly quantitative relationship.

PROTEINS

Ellinger [31] is said to have reported abnormal serum proteins first in cases of this disease in 1899. Feller and Fowler [32] listed 52 cases of elevated serum protein in multiple myeloma as collected through 1936 and noted that most of them had appeared since 1928. By 1937 the number had risen to 60,[33] and Jeghers and Selesnick [34] had concluded that hyperproteinemia occurred in between 50 and 60 per cent of cases of multiple myeloma.

Causes of hyperproteinemia, which almost always means hyperglobinemia, as observed by several authors,[35] are shown in table 3.

The reason for this increased serum protein level in cases of multiple myeloma is not known, although the bone marrow and the liver have both been implicated. In 1 of our cases the myeloma cells in the bone marrow peculiarly resembled reticulum cells involved in a storage disease.

The only unusual observation with respect to the spinal fluid of which we are cognizant is that reported in the Cabot case, number 20031,[36] in which the gold sol curve was 5555555554 and the protein was 95 mg. per hundred cubic centimeters.

Precipitation of this protein by Hayem's solution [37] and by cold [15] has been noted occasionally. The relationship between the elevated serum globulin, formation of rouleaux and an increased sedimentation rate has been mentioned.

Of the 83 cases in this series estimations of total serum protein were made in 55 cases. In 40 of these (73 per cent) the concentration of protein was elevated above a level of 8.0 Gm. per hundred cubic centimeters. In all but 3 of these there was a reversal of the albumin-globulin ratio. The highest serum protein value obtained was 14.1 Gm. per hundred cubic centimeters, with an albumin-globulin ratio of 1:3.3. The most disproportionate ratio (1:6.7) occurred with a serum protein of 11.8 Gm.

In 40 cases in which the concentration of protein in the serum was elevated there were multiple roentgenographic changes in 73 per cent, osteoporosis in 15 per cent and no roentgenographic changes in 12 per cent. The concentration of hemoglobin was less than 13.5 Gm. in 100 cc. of blood in all cases and less than 11 Gm. in 90 per cent of cases. Bence-Jones proteinuria was present in 56 per cent of cases. The sedimentation rate (Westergren method) was 100 mm. or more in one hour in 97 per cent of the 40 cases.

CALCIUM

In 1936 Gutman and his co-workers [38] reviewed the cases of multiple myeloma in the literature in which determinations of blood calcium had been made. Seventy-two cases were found at that time, and to these they added 6 of their own. The calcium values as recorded were elevated (more than 12 mg. per hundred cubic centimeters) or said to be elevated in 34 instances (44 per cent). The highest value was 20.0 mg. per hundred cubic centimeters. In 4 of their 6 cases the levels were elevated.

As a rule the serum phosphorus is normal or slightly elevated and the phosphatase is normal or somewhat increased. Two different authors reported serum phosphorus values of 6.8 mg. per hundred cubic centimeters.

TABLE 3.—*Causes of Hyperproteinemia*

Cause	Frequency of Hyperproteinemia	Protein, Gm. in Each 100 Cc. of Serum	Author
Kala-azar	....	10.54	Wu
Syphilis	....	9.37	Wu
Renal carcinoma	....	.....	Peters and Eisenman
Lymphosarcoma	....	.....	Feller and Fowler
Schistosomiasis	50%	8 to 10	Meleney and Wu
Leprosy (32 cases)	80%	Over 8	Frazier and Wu
Cirrhosis	....	11.46	Snapper
Chronic nephritis	....	9.14	Snapper
Lymphogranuloma venereum	62 of 67 cases	Over 8	Kagan
Dehydration	....	.....	Kagan
Monocytic leukemia	....	.....	Kagan
Boeck's sarcoid	....	.....	Kagan

TABLE 4.—*Data for Cases in Which Serum Calcium Was Greater than Normal*

Case	Calcium, Mg. in Each 100 Cc. of Serum	Phosphorus, Mg. in Each 100 Cc. of Serum	Phosphatase, Bodansky Units	Protein, Gm. in Each 100 Cc. of Serum
1	13.8	2.9	...	....
2	12.3	3.0	...	7.7
3	15.6	3.8	0.9	13.5
4	12.5	3.0	2.4	11.4
5	15.7	6.6	...	8.1
6	15.9	4.0	...	6.4
7	12.7	2.9	1.9	9.5
8	12.9	6.0	2.2	6.5

In our series determinations of serum calcium were obtained in 41 instances, of serum phosphorus in 36 cases and of alkaline phosphatase (Bodansky) in 24 cases. In only 8 instances did the serum calcium exceed 12.0 mg. per hundred cubic centimeters in this group (20 per cent). The highest values were 15.6, 15.7 and 15.9 mg. per hundred cubic centimeters.

The serum phosphorus averaged 3.41 mg. per hundred cubic centimeters, ranging from 0.8 to 14.3 mg. per hundred cubic centimeters. Twenty-eight of the 36 estimations were between 0.8 and 4.2 mg. per hundred cubic centimeters.

The alkaline phosphatase ranged between 0.8 and 12.3 units (Bodansky) and averaged 3.02 units. Twenty-one of the twenty-four determinations were found to be within 0.8 and 3.6 units and averaged 2.13 units.

31. Ellinger, A., cited by Wintrobe and Buell.[15]
32. Feller, A. E., and Fowler, W. M.: Hyperproteinemia in Multiple Myeloma, J. Lab. & Clin. Med. **23**: 369-378 (Jan.) 1938.
33. Atkinson, F. R. B.: Multiple Myelomata, M. Press **195**: 312 (Oct. 6), 327 (Oct. 13) 1937.
34. Jeghers, H., and Selesnick, S.: Hyperproteinemia: Its Significance, Internat. Clin. **3**: 248-279 (Sept.) 1937.
35. (*a*) Snapper.[15] (*b*) Feller and Fowler.[32] (*c*) Jeghers and Selesnick.[34] (*d*) Peters, J. P., and Eisenman, A. J.: The Serum Proteins in Diseases Not Primarily Affecting the Cardiovascular System or Kidneys, Am. J. M. Sc. **186**: 808-833 (Dec.) 1933. (*e*) Kagan, B. M.: Hyperglobulinemia, Am. J. M. Sc. **206**: 309-315 (Sept.) 1943. (*f*) Meleney, H. E., and Wu, H.: The Blood Serum Globulin in Schistosomiasis Japonica, China M. J. **38**: 357-361 (May) 1924. (*g*) Wu, H.: A New Colorimetric Method for the Determination of Plasma Proteins, J. Biol. Chem. **51**: 33-39 (March) 1922.
36. Multiple Plasma Cell Myeloma Involving Sternum, Brain, Skull and Kidney, Cabot Case 20031, New England J. Med. **210**: 154-158 (Jan. 18) 1934.
37. Feller and Fowler.[32] Jacobson, B. M.: On a Peculiar Serum Protein Precipitated by Hayem's Solution Occurring in Multiple Myeloma, Proc. Soc. Exper. Biol. & Med. **32**: 1257-1258 (May) 1935.
38. Gutman, A. B.; Tyson, T. L., and Gutman, E. B.: Serum Calcium, Inorganic Phosphorus and Phosphatase Activity in Hyperparathyroidism, Paget's Disease, Multiple Myeloma and Neoplastic Disease of the Bones, Arch. Int. Med. **57**: 379-413 (Feb.) 1936.

When those cases are listed in which the serum calcium was found to be elevated (table 4), it will be seen that the values for serum phosphorus were either normal or slightly elevated and that the phosphatase activity, when noted, was normal to low. It will also be noted from table 4 that no apparent correlation exists between the serum calcium level and that of the serum protein.

RENAL COMPLICATIONS

Many patients who have multiple myeloma are first given a diagnosis of nephritis, and many more patients manifest renal impairment at some stage of their disease. In some cases uremia is the terminal event. The presenting complaint may be that "my urine is loaded with albumin."

In Bell's review of the subject in 1933 [39] he stated that the only direct effect of multiple myeloma on the kidneys was obstructive, owing to tubular casts of Bence-Jones protein and atrophy. He expressed the opinion that Bence-Jones proteinuria per se does not have an injurious effect on either the glomerulus or the tubule. Others have noted this same lesion, which has been called "intranephritic hydronephrosis." [26e]

In those cases in which Bence-Jones proteins did not seem to be incriminated, Bell felt that renal failure could be explained on another basis than multiple myeloma.

In 5 of our cases albuminuria was the outstanding symptom on admission. Of the few patients that have died while still here, uremia was a part of the terminal episode in 3 instances.

Fifty-one patients in this group (61 per cent) exhibited varying degrees of renal impairment as evidenced by albuminuria (grade 2 or more on a basis of 1 to 4) with or without casts, red blood cells or an elevated blood urea. A third of these patients had albuminuria alone.

SOLITARY MYELOMAS

In the 10 cases represented in this group of solitary myelomas, the myelomas are not unequivocally solitary, but they are doubtfully multiple, and because these lesions tend to bear a somewhat better prognosis than the multiple ones they have been reviewed separately. Another group of 11 cases of solitary myelomas involving the oronasal cavities have recently been reported elsewhere.[7]

However, this separation of multiple and solitary myelomas is to some degree artificial because they are probably all a phase in the same disease in which the plasma cell leukemias represent one extreme and the solitary myelomas the other. Furthermore, "solitary myeloma" is frequently an inexact designation, since a single lesion determined by roentgenography, even when a sternal aspiration has been negative in result, is not complete assurance of a solitary process.

Tennent,[40] in a review of 49 solitary myelomas of bone which he found in the literature, stated that 30 per cent of them became generalized. This is somewhat at variance with the opinion expressed [41] that this form of myeloma is benign. Likewise Figi, Broders and Havens [7] have emphasized the malignant character of the extramedullary myelomas which they reported.

In King's case [42] of a solitary intraosseous lesion, multiple myeloma manifested itself four years later. Jackson and Parker [10b] reported a case (number 1) of an extramedullary myeloma which became generalized ten years after the patient's initial biopsy.

In Geschickter's case [43] of a solitary myeloma, demonstrated in the left hip by roentgenography, the patient pursued a progressive downhill course regardless of the fact that no generalized disease could be demonstrated.

Cutler and others [44] collected reports of 12 cases of solitary intraosseous myeloma from the literature and 5 from the bone registry, and added 1 of their own. Of the 5 patients having Bence-Jones proteinuria, 4 showed a generalized spread within two months to four years thereafter. Of those without Bence-Jones proteinuria, 1 was alive and apparently well four years later, 1 nine years later and 1 ten years.

Pasternack and Waugh [45] reported a case in which the patient was alive and without a generalized spread of the disease after seven and a half years.

In 1943, Hellwig [46] collected the cases of extramedullary plasma cell tumors from the literature and added 1 of his own for a total of 128 cases. Of the cases that he collected 47 were conjunctival, benign and probably inflammatory. Four were nodal. Two of these were associated with typical multiple myeloma and 1 with other involved viscera. Thirteen involved other organs. Sixty-three were in the air passages. These Hellwig divided into five groups. Group 1 included 26 patients who had single tumors which were felt to be "noncancerous." None of the patients had Bence-Jones proteinuria and none of the tumors was known to have become generalized. The nine tumors in group 2 were "noncancerous and multiple." Three of 7 recurred. The tumors in group 3 were "cancerous without metastasis." Of the 10 patients most died within a year. One was alive after twelve years. In group 4 there were 9 patients, with tumors "cancerous with metastases in nodes." All patients died shortly thereafter. In group 5 there were 9 patients, with tumors "cancerous with metastases to bone." All patients died, but over a period of twelve years. Bence-Jones protein appeared with involvement of bone.

In 1 of the cases of oronasal myeloma reported by Figi, Broders and Havens[7] from the Mayo Clinic in June 1945, the patient was a man of 60 years of age who came to the clinic in July 1934, complaining of a choking sensation in his throat. A myeloma measuring 4 by 3 by 2 cm. and involving the right tonsil was removed, and two courses of roentgen therapy were administered. His urine did not show evidence of Bence-Jones protein.

In June, 1942, the patient returned with a six weeks' history of pain in his sternum and ribs anteriorly, and of a loss of 8 to 10 pounds (3.6 to 4.5 kg.). A roentgenogram of the thorax revealed multiple osteolytic lesions. Bence-Jones protein was demonstrated in his urine. He died four months later.

It therefore becomes apparent that the benignancy of these solitary myelomas is only relative, that they are intimately associated with what it is customary to refer to as multiple myeloma, if not indeed a part of the same process, and that fairly frequently the full-

39. Bell, E. T.: Renal Lesions Associated with Multiple Myeloma, Am. J. Path. **9**: 393-419 (July) 1933.
40. Tennent, W.: Plasmocytoma of Bone, Brit. J. Surg. **32**:-471-476 (April) 1945.
41. Editorial: The Problem of Myeloma, J. A. M. A. **104**: 1420-1421 (April 20) 1935.
42. King, B. B.: Solitary Plasma Cell Myeloma of Bone as an Initial Stage of Multiple Myeloma, J. A. M. A. **115**: 36-38 (July 6) 1940.
43. Geschickter, C. F.: Multiple Myeloma as a Single Lesion, Ann. Surg. **92**: 425-433 (Sept.) 1930.
44. Cutler, M.; Buschke, F., and Cantril, S. T.: The Course of Single Myeloma of Bone (A Report of Twenty Cases), Surg., Gynec. & Obst. **62**: 918-932 (June) 1936.
45. Pasternack, J. G., and Waugh, R. L.: Solitary Myeloma of Bone: Clinical and Pathologic Entity, Ann. Surg. **110**: 427-436 (Sept.) 1939.
46. Hellwig, C. A.: Extramedullary Plasma Cell Tumors as Observed in Various Locations, Arch. Path. **36**: 95-111 (July) 1943.

blown picture of multiple myeloma develops, even following successful excision of the local lesion without local recurrence.

Another of our patients, a man of 44 years, registered at the clinic in December 1944, because albumin had been discovered in a routine examination of the urine. It contained Bence-Jones protein when examined at the clinic, although roentgenograms of his skull, thorax, spinal column, pelvis and femurs revealed only a small, single defect in his skull. However, a smear of the sternal marrow yielded 6 per cent of myeloma cells, to establish as multiple myeloma what otherwise might have passed for a solitary myeloma. A more recent report on the patient from his home physician stated that within three months after the patient had left the clinic a second lesion had appeared in the femur and 95 per cent of myeloma cells were present in a smear of the sternal marrow. This is an instance of an apparent, not a real solitary myeloma.

It may be of some interest to note here also that since we have begun doing sternal aspirations routinely on these patients, we have not encountered any solitary myelomas. This does not mean that we doubt their occurrence. We do, however, feel that more of the so-called solitary myelomas will be found to be part of a diffuse process as more care is taken to establish the diagnosis.

The pertinent available data on the 10 cases of solitary lesions are listed in table 5. In no instance had the additional confirmation been obtained of a sternal aspiration with negative result.

DIAGNOSIS

The various clinical and laboratory features of this disease are striking, and the occurrence of multiple osteolytic lesions of the bone, Bence-Jones proteinuria and hyperproteinemia is strongly suggestive evidence for the presence of multiple myeloma. However, every effort should be made to confirm this with pathologic material for the sake of accuracy of prognosis and suggestions as to an outline of treatment. To this end, because of its simplicity and broad diagnostic range, the method of sternal aspiration readily lends itself. Beizer and his co-workers,[20e] Young and Osgood,[47] and others have discussed this in detail elsewhere.

With regard to the use of sternal aspiration it must be mentioned that a negative result is not always adequate evidence for excluding the possibility of multiple myeloma. The changes in the bone marrow may be irregularly distributed rather than diffuse, and the results on repeated aspirations are not uniform. In 1 instance a third aspiration of marrow was necessary to secure a diagnostic specimen.

TREATMENT

Unfortunately, there is as yet nothing of proved worth, either curative or palliative, to be offered to patients who have multiple myeloma. Coley's[12] toxin, roentgen therapy and radioactive phosphorus have been tried by ourselves and others with indifferent results, though occasionally with relief of pain. More recently radioactive strontium has been used. Nothing is known of the comparative value of this substance and radioactive phosphorus at present.

One of our patients was put on a high calcium regimen[48] in 1941 and wrote two years later that she was mowing the lawn and doing her own housework and "felt better than she had in ten years." When last heard from in October 1945, fifty-one months after the diagnosis had been established, she was hospitalized for a fracture of her left femur and had not taken any calcium for two years. However, we have reason to believe that this patient had a more chronic form of the disease than most.

Batts[9] reported on 3 patients who underwent laminectomy for decompression of the spinal cord after the development of paraplegia. One died postoperatively, 1 reported herself well at the end of three months and 1 died of pneumonia four years after his operation without evidence of recurrence. A patient on whom operation was performed at the clinic was relieved of paraplegia by removal of an apparently local lesion which had caused compression of the first lumbar vertebra. The patient lived seven and a half years thereafter. The ultimate cause of death was not known.

TABLE 5.—*Data on Cases of Solitary Lesions*

Age, Yrs.	Sex	Site of Tumor	Bence-Jones Protein	Roentgenographic Changes	Duration, Mos.	Diagnosed by
23	F	Left femur	—	None in skull, thorax or spinal column	42	Biopsy
15	M	Fifth lumbar vertebra	..	None in thorax or spinal column; compression in fifth lumbar vertebra	4	Necropsy
40	M	Second thoracic vertebra	..	Compression in second thoracic vertebra	21	Biopsy
55	F	Left hip	—	None in skull, thorax or left ilium	29	Biopsy
43	M	Left clavicle	—	.....	66	Biopsy
54	M	Right scapula	—	In right scapula; none in skull	66	Biopsy
44	M	Right femur	—	In right femur; none in skull or thorax	15	Biopsy
68	M	Presacral	—	None in thorax, spinal column or extremities	108	Biopsy
49	M	Seventh thoracic vertebra	..	None in thorax; compression in seventh thoracic vertebra	36	Biopsy
38	M	Fifth lumbar vertebra	—	None in skull or thorax; compression in fifth lumbar vertebra	102	Biopsy
42.9 *					49 *	

* Average.

PROGNOSIS

Fifty-five patients in this group were followed until the time of their death. For 11 others who are still living, follow-up reports are available.

Of the 55 who died, the average duration of the disease from the onset of symptoms was eighteen and eight-tenths months. The median duration was fifteen months. The longest period of survival was eighty-four months, and the shortest was one month.

The usual duration of symptoms before the patient's first visit to the clinic was eight months, and the expectation for survival thereafter averaged ten months and varied between one week and seventy-two months. The median was somewhat less, with 50 per cent of the patients failing to live throughout the first half year afterward. No correlation between life expectancy and the form of treatment was noted.

In 27 cases in which the serum proteins were found to be elevated the average duration was eighteen and one-tenth months and the average survival after examination was six and one-tenth months.

47. Young, R. H., and Osgood, E. E.: Sternal Marrow Aspirated During Life: Cytology in Health and in Disease, Arch. Int. Med. **55**: 186-203 (Feb.) 1935.

48. Calcium gluconate and calcium lactate in equal parts, 20 grains (1.3 Gm.), was administered four times a day for one month, three times a day for one month and thenceforth twice a day. Calcium gluconate, 10 cc. of a 10 per cent solution, was administered intravenously every other day for sixteen doses simultaneously with the beginning of oral administration.

Of 30 patients having Bence-Jones proteinuria who were followed, the duration of the disease averaged twenty-three and seven-tenths months and ranged from one month to seven years.

Although, as can be seen, neither the serum protein nor Bence-Jones proteinuria has any prognostic value, we believe that a distinction between acute and chronic multiple myeloma may be made cytologically on the basis of the smear of the sternal aspiration. This we hope to be able to report on in detail later.

CAUSATION

At present there exists a rather wide diversity of opinion regarding the nature of the parent myeloma cell and the types of multiple myeloma to be found.

It has been suggested that myeloma cells arise from supportive tissue, not marrow,[49] that they arise from myeloblasts,[50] erythroblasts,[51] osteoblasts [52] or the reticuloendothelial cells,[53] or that they are modified lymphoid tissue.[54] Although we have seen myeloma cells which resembled immature red cells and others which looked like stem cells, we have felt that in more malignant lesions, where the younger cells occurred with greater frequency, we could trace their origin to the reticuloendothelial cells. Thus it seems likely to us that myeloma cells arise from the reticuloendothelial cells and develop through a dysplastic plasma cell line, which rarely matures and probably does not produce a true plasma cell when it does mature.

Many observers have felt that in addition to the "plasma cell" type of myeloma, "plasmacytoma," there exist "lymphocytomas," [55] "myeloblastomas," "erythroblastomas" [56] and "myelocytomas." [57] Christian, who has been repeatedly quoted as supporting the plasma cell type of multiple myeloma, has since stated in a discussion of a paper presented by Giffin, Beizer and Hall [58] that the type of myeloma cell may range between the myelocyte on one hand and the plasma cell on the other. Rosenthal and Vogel's [23] case of a myelocytoma (number 13) is the only case of multiple myeloma of which we have knowledge that was identified as other than a plasma or myeloma cell type by the method of sternal aspiration. All others were made from fixed tissue sections. Even in Rosenthal and Vogel's case the few myeloma cells present were essential to the diagnosis. This implies the possibility that it was actually a myeloma cell type with a leukemoid reaction and that further efforts to secure specimens of marrow might have yielded a different spread of cells.

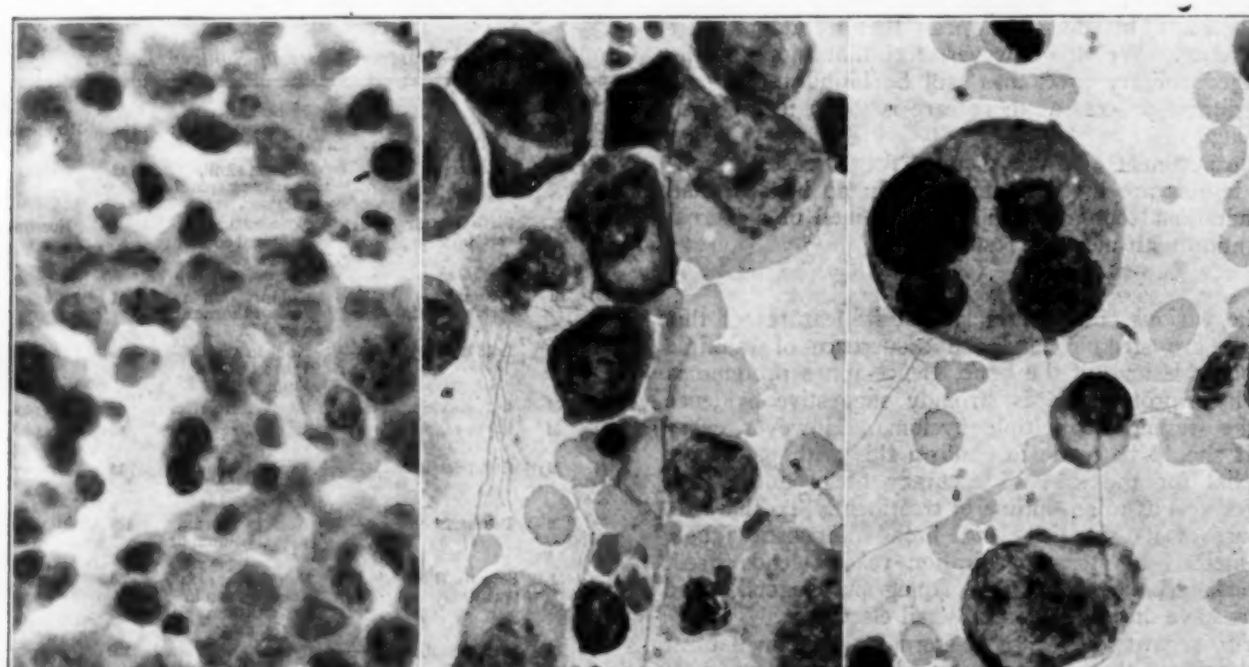

Fig. 7.—(*a*) Fixed section of the sternal marrow presents a picture such as is usually referred to as a "myeloblastoma," whereas smears of the same marrow (*b* and *c*) reveal a highly malignant "plasma cell" myeloma.

In 1 case in this series the lesion was reported by the pathologist from a biopsy specimen as a myeloblastoma. In another, not included in this report, the lesion was previously considered to be a multiple myeloma occurring in a 4 year old child. The report at necropsy was multiple myeloma in which only myeloblastic cells were seen. A review of this case makes a diagnosis of leukopenic leukemia seem more probable.

Every one of the 49 cases so diagnosed by sternal aspiration has been without exception of the myeloma

49. Ewing, J.: Neoplastic Diseases: A Treatise on Tumors, ed. 3, Philadelphia, W. B. Saunders Company, 1928, pp. 321-327.

50. (*a*) Ewing.[49] Snapper.[21] (*b*) Multiple Myeloma, Cabot Case 21012.[20c] (*c*) Kaufmann, E.: Pathology for Students and Practitioners, translated by S. P. Reimann, Philadelphia, P. Blakiston's Son & Co., 1929, vol. 2, pp. 1216-1222.

51. (*a*) Ross, Discombe and Robb-Smith.[20b] (*b*) Meyer, Halpern and Ogden.[20] (*c*) Editorial.[41] (*d*) Ewing.[49] (*e*) Vance, B. M.: A Case of Multiple Myelomata with a Discussion as to Its Nature and Origin, Am. J. M. Sc. **152**: 693-714 (Nov.) 1916. (*f*) Jordan, H. E.: On the Genetic Relation Between So-Called Plasma Cells and Erythroblasts in Certain Lymph Nodes, Anat. Rec. **42**: 91-108 (April 25) 1929.

52. Williams, H. W.: Multiple Myeloma of Bone: Report of Two Cases with Remarks on Histogenesis, Am. J. Cancer **16**: 540-555 (May) 1932.

53. Beizer, Hall and Giffin.[20a] Lowenhaupt.[27] Scott, E.; Stanton, F. M., and Oliver, M.: Multiple Myeloma: A report of Five Cases, Am. J. Cancer **17**: 682-698 (March) 1933. Doan, C. A., cited by Scott, Stanton and Oliver.

54. Jackson, Parker and Bethea.[20b] Stewart and Weber.[20d]

55. Batts.[9] Stewart and Weber.[20d] Vance.[51e]

56. Meyer, Halpern and Ogden.[20] Kaufmann.[50c] Vance.[51e] Jordan.[51f]

57. Rosenthal and Vogel.[23] Kaufmann.[50c] Christian, H. A.: Multiple Myeloma: A Histological Comparison of Six Cases, J. Exper. Med. **9**: 325-351 (July 1) 1907.

58. Giffin, H. Z.; Beizer, L. H., and Hall, B. E.: The Diagnosis of Multiple Myeloma by Sternal Aspiration, Tr. A. Am. Physicians **56**: 364-370, 1941.

cell type. One of the more recent of these was a myeloma cell type of a high degree of malignancy with many immature forms appearing on the smear of bone marrow. The fixed tissue sections of the same marrow for this patient resembled what has usually been referred to as "myeloblastoma" (fig. 7).

It is for these reasons that we have come to regard the myeloma cell as a specific type associated with multiple myeloma.

Some have disputed whether or not this disease is (1) a form of cancer, (2) a form of leukemia or (3) a form of lymphoma. Its various features give it a resemblance to each of the classifications mentioned, but as long as its clinical and pathologic manifestations are kept in mind, it is of little moment at this time which thesis one supports.

SUMMARY

The clinical and clinical laboratory data in 83 cases of pathologically confirmed multiple myeloma were reviewed, and the opinion is expressed that this disease is represented by a single cell type arising from the reticuloendothelial system in a dysplastic plasma cell line. Multiple myeloma is a uniformly malignant and usually rapidly fatal disease in its generalized form and ranges from the solitary to the leukemic stage at either extreme. Confirmation of the diagnosis is important, and sternal aspiration is most probably the method of choice. By use of this procedure some additional indications of chronicity or acuteness may be derived. Thus far an effective form of therapy has not appeared.

STILBAMIDINE AND PENTAMIDINE IN MULTIPLE MYELOMA

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Antimony compounds cure kala-azar, a disease which is accompanied with an increase in the globulin content of the serum.[1] Because of this association, antimony compounds have been tried in other diseases in which hyperglobulinemia occasionally occurs. These preparations have been given in Hodgkin's disease, leukemia and multiple myeloma, but until now favorable reports have not appeared in the literature.

Since 1939 diamidine compounds not containing antimony have been successfully employed in the treatment of kala-azar.[2] This report deals with the influence of two diamidine compounds, Stilbamidine (4,4-diamidinostilbene) and Pentamidine (4,4'-[pentamethylenedioxy]dibenzamidine),[3] on multiple myeloma, a disease in which increase of the globulin content of the serum is of frequent occurrence.[4]

For 13 patients with multiple myeloma the administration of Stilbamidine, combined with a diet low in animal protein, has had a favorable influence on the pain which is characteristic of this disease. For 2 patients with myeloma good results were obtained by the injection of Pentamidine. Until now, neither drug has influenced the course of multiple myeloma for patients who were fed a diet high in protein.

METHOD

Stilbamidine was given either intravenously or intramuscularly. The intramuscular route was chosen only when veins were not readily available for injection. For intramuscular injection the diamidinostilbene was dissolved in 5 cc. of 2 per cent solution of procaine hydrochloride. For intravenous injection, the compound was dissolved in 10 cc. of distilled water. The solution should not be autoclaved.

The dosage schedule was as follows: A first injection of 50 mg. was given, followed two days later by an injection of 100 mg. Thereafter 150 mg. was given, usually every other day but in some cases daily. At first the treatment was limited to fifteen injections of 150 mg. In the later cases the injections were continued until a total dose of 4 to 5 Gm. had been given. In most cases of kala-azar, ten injections of 150 mg. of Stilbamidine are sufficient for cure. Exceptionally, even in kala-azar,[5] larger doses have been necessary. Pentamidine was given every other day in intramuscular injections of 100 mg. dissolved in 5 cc. of distilled water. The total dosage given varied between 2 and 3 Gm.

Table 1 illustrates the diet poor in animal protein as prescribed. Theoretically the diet of these patients should consist mainly of milk, cheese, wheat, wheat gluten and corn. However, practical application renders dietary concessions necessary.

The literature stresses the fact that injections of Stilbamidine are often followed by a fall in blood pressure which on occasion may lead to sweating, dizziness, nausea and even collapse. For this reason it has been advised that 0.25 cc. of a 1 in 2,000 solution of epinephrine be injected subcutaneously ten minutes before the injection of Stilbamidine.[6] In patients with myeloma the injections of epinephrine caused more complaints than the injections of Stilbamidine! To a few patients, when sweating and dizziness were noticed after the injection, $\frac{1}{150}$ to $\frac{1}{200}$ grain (0.43 to 0.33 mg.) of atropine sulfate was given before the Stilbamidine with good results. Many patients notice a sensation of formication immediately after the injection.

One late sign of intoxication, dissociated anesthesia in the area supplied by the trigeminal nerve, may occur several months after the treatment.[6] This is accompanied with loss of sensation to light touch, whereas the sensations of pain, temperature and pressure are usually preserved. This facial anesthesia begins two and one-half to five months after the treatment has ended. It lasts one or more months but has a tendency to spontaneous recovery. My colleagues and I have observed this dissociated anesthesia in 4 of 20 patients treated with Stilbamidine. It may well be advisable to

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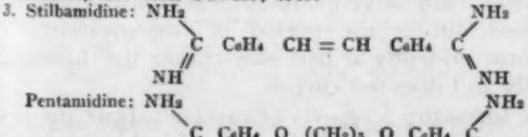
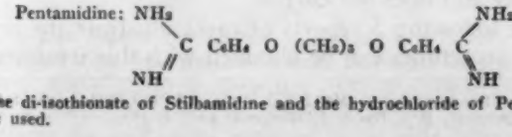
Stilbamidine and Pentamidine are manufactured by May and Baker, Dagenham near London, England. The two compounds used in this study were supplied by Merck and Co., Inc., Rahway, N. J., through the courtesy of Dr. D. F. Robertson.

1. Snapper, I.: Chinese Lessons to Western Medicine, New York, Interscience Publishers, Inc., 1941.
2. Lourie, E. M., and Yorke, W.: Ann. Trop. Med. **33**: 289, 1939. Adams, A. R. D., and Yorke, W.: ibid. **33**: 323, 1939. Adler, S., and Rachmilewitz, M.: ibid. **33**: 327, 1939.
3. Stilbamidine: NH_2 ... NH_2



Pentamidine: NH_2 ... NH_2



The di-isothionate of Stilbamidine and the hydrochloride of Pentamidine were used.

4. Snapper, I.: Medical Clinics on Bone Diseases, New York, Interscience Publishers, Inc., 1943.
5. Kirk, R., and Sati, M. H.: Ann. Trop. Med. **37**: 34, 1943. Susskind, S.: ibid. **37**: 158, 1943.
6. Napier, L. E., and Sen Gupta, P. C.: Indian M. Gaz. **77**: 71, 1942; **78**: 177, 1943.

protect these patients from sunlight during and after the treatment.

In patients with renal failure the drug has to be given with great caution.

RESULTS

Fifteen patients with multiple myeloma have been treated to date with injections of Stilbamidine or Pentamidine combined with a diet low in animal protein. Eleven patients were treated with Stilbamidine alone, and 1 patient with Pentamidine alone. In 1 patient Stilbamidine did not influence the pain, but a highly satisfactory result was obtained when Pentamidine was given instead of Stilbamidine. For 2 patients Pentamidine was ineffective, but the pain disappeared after treatment with Stilbamidine. For the time being, therefore, both compounds seem to have a place in the treatment of multiple myeloma, although as a rule Stilbamidine is the more effective preparation.

All these patients were suffering excruciating pains when the treatment was begun. Thirteen were immobilized in bed. All 15 improved considerably as far as the pain itself was concerned. Eleven could walk at the time of discharge from the hospital. One patient had paraplegia due to compression of the cord by myeloma before treatment was begun. The pains in the upper part of the body disappeared during the treatment but, as was to be expected, the mobility of the legs did not return. In 1 patient who, one month after termination of treatment, was able to walk around freely and practically without pain, diabetic coma suddenly developed and proved fatal. Two other patients died, 1 of uremia due to myeloma of the kidneys and 1 of thrombopenia. In both the pains had disappeared.

Table 2 shows the quantities of Stilbamidine and Pentamidine given in the first 12 cases.

In 3 of the 15 cases the possible influence of roentgenologic treatment requires discussion. One patient had been treated unsuccessfully with small doses of roentgen irradiation (1,200 r) immediately before the treatment with Stilbamidine was begun. In the second case there was a transverse lesion of the spinal cord; the vertebral column was irradiated during the treatment with Stilbamidine. A third patient had been treated without success with large doses of roentgen irradiation (2,400 and 3,000 r) eight months before admission to the Mount Sinai Hospital. Here she became completely free of pain after treatment with Stilbamidine. Thereupon small doses of roentgen irradiation (1,200 r) were given in the hope that recalcification would be stimulated. The other patients did not receive roentgen irradiation during or after the treatment with diamidine compounds. During the treatment with Stilbamidine morphologic changes develop in the myeloma cells,[7] consisting of precipitates of ribose nucleic acid. The possibility has to be considered that these changes in the nucleoprotein of the cytoplasm of the myeloma cells may render these cells more vulnerable to roentgen rays.

The remarkable clinical improvement has persisted in 1 case for eighteen months. Another patient who after treatment with Stilbamidine was entirely free of symptoms had a relapse sixteen months after the first treatment. Subsequent treatment with Pentamidine was ineffective, but the pains disappeared after renewed treatment with Stilbamidine. In 1 other case the improvement has now lasted for eight months. In other patients relapses of pain have occurred which usually could be treated successfully with a new series of Stilbamidine injections.

Of the 15 patients treated, 2 had Bence-Jones proteinuria with hyperglobulinemia, 4 had Bence-Jones proteinuria without hyperglobulinemia, 4 had hyperglobulinemia without Bence-Jones proteinuria and 5 had neither Bence-Jones proteinuria nor hyperglobulinemia.

The diagnosis of multiple myeloma in these cases was definitely established by punctures of the sternal marrow and biopsies. All subsequent examinations of the marrow proved that even during the period of great improvement and subjective well-being large numbers of myeloma cells were still present. As was mentioned before, the myeloma cells of the patients treated with Stilbamidine showed specific changes;[7] nevertheless the number of these cells did not decrease significantly. In the urine of patients who excreted Bence-Jones protein this abnormal substance persisted. The abnormally large globulin content of the serum also remained during the period of improvement. The treatment evidently at best only checks the disease temporarily and does not cure it.

The following 3 reports of cases illustrate the results which sometimes can be obtained with this treatment.

TABLE 1.—*Diet Poor in Animal Protein*

Tuesday

Carbohydrate 171; protein 64; fat 60; 1,480 calories

Breakfast	Dinner	Supper
1 orange	1 cup cream potato soup	½ cup vegetable soup
½ cup maltex	2 oz. meat loaf	½ cup spaghetti creole
1 boiled egg	½ cup mashed potato	½ cup peas
1 slice toast	½ cup beets	2 slices bread
1 teaspoon butter	1 baked custard	2 teaspoons butter
1 cup coffee	1 slice bread	8 oz. milk
1 teaspoon sugar	1 teaspoon butter	1 slice watermelon
1 oz. (28.3 Gm.) milk	8 oz. (227 Gm.) milk	

Wednesday

Carbohydrate 161; protein 76; fat 78; 1,650 calories

Breakfast	Dinner	Supper
3 prunes	1 cup tomato bouillon	1 cup cream celery soup
½ cup farina	2 oz. (57 Gm.) beef stew	1 hard cooked egg
1 boiled egg	1 lettuce heart	2 oz. cottage cheese
1 slice toast	1 slice bread	1 baked potato
1 cup coffee	1 teaspoon butter	1 serving lettuce and tomato
1 oz. milk	8 oz. milk	1 blueberry muffin
1 teaspoon sugar	1 serving ice cream	1 teaspoon butter
1 teaspoon butter		1 teaspoon sugar
		1 slice bread
		8 oz. milk

Thursday

Carbohydrate 236; protein 69; fat 65; 1,805 calories

Breakfast	Dinner	Supper
½ cup applesauce	1 cup vegetable soup	1 cup consomme
1 cup dry cereal	2 oz. pot roast	½ cup string beans
1 boiled egg	½ cup mashed potato	1 steamed potato in jacket
1 slice toast	½ cup peas	½ cup carrots
1 teaspoon butter	3 fresh plums	½ cup beet salad
1 cup coffee	1 slice bread	2 slices bread
1 oz. milk	1 teaspoon butter	2 teaspoons butter
1 teaspoon sugar	8 oz. milk	8 oz. milk
		1 plain cake

Friday

Carbohydrate 213; protein 87; fat 116; 2,224 calories

Breakfast	Dinner	Supper
3 prunes	1 cup cream tomato soup	1 cup cream spinach soup
½ cup farina	2 oz. boiled fish	2 eggs
1 boiled egg	1 steamed potato in jacket	2 teaspoons mayonnaise
1 slice toast	½ cup peas	1 oz. cottage cheese
1 teaspoon butter	1 slice bread	1 baked potato
1 oz. milk	1 teaspoon butter	1 green salad
1 cup coffee	8 oz. milk	2 slices bread
1 teaspoon sugar	1 serving ice cream	2 teaspoons butter
		8 oz. milk
		2 oatmeal cookies

7. (*a*) Snapper, I.: J. Mt. Sinai Hosp. **14**: 119, 1946. (*b*) Snapper, I., and Schneid, B.: Blood, J. Hematol. **1**: 534, 1946.

REPORT OF CASES

CASE 1.—J. G., a man 59 years old, was admitted to the Mount Sinai Hospital on January 23, 1945, because of pains in the back radiating to both legs and feet. In the course of the previous year the patient had lost 35 pounds (15.9 Kg.). The pain had been progressive and for several months had disturbed his sleep. He had been admitted previously to two other hospitals, but the pains had become steadily worse.

On admission the patient could move only with difficulty in bed; he complained continuously of pain. Physical examination showed considerable tenderness of the bones and enlargement of the liver and the spleen.

The hemoglobin was 50 per cent. There were 8,800 white blood cells with a normal differential count. The sedimentation rate was 135 mm. per hour (Westergren method). The urine did not contain Bence-Jones protein. The blood serum contained 10.3 mg. of calcium per hundred cubic centimeters, 5.3 mg. of inorganic phosphorus and 16 King-Armstrong units of phosphatase. The total proteins in the serum were 6.5 Gm. per hundred cubic centimeters, with 3.8 Gm. of albumin and 2.7 Gm. of globulin. The formaldehyde gel reaction was negative.

On roentgenologic examination numerous small areas of rarefaction were seen throughout the calvarium. There were many osteophytes in the spine. The pedicles of the thoracic vertebrae were poorly outlined due to osteoporosis. In the pelvis many areas of rarefaction were seen. There was a large, gaping, incomplete fracture of the head of the right femur.

Sternal marrow aspiration showed 52 per cent plasma cells.

Between February 7 and February 23 the patient received six treatments of 200 r each to the lumbar spine and six treatments of 200 r to the sacrum. This treatment had no effect on the pains.

Between February 18 and March 20 nineteen intravenous injections of Stilbamidine were given, totaling 2,500 mg. The first decrease in the pain was noticed about the middle of March, after twelve injections had been given. Thereafter the improvement advanced rapidly. At his discharge, on April 4, the patient walked out of the hospital almost like a normal man. Shortly afterwards he resumed his activities as a porter, and he has been working until now (October 1946) without interruption. His general condition is excellent. He is far stronger than the average person; he currently carries heavy loads on his shoulders and shifts weighty burdens without difficulty.

In this patient the disease is evidently arrested. Repeated roentgenologic examinations reveal that none of the osteolytic areas demonstrated in February 1945 have enlarged to date (May 1946). Most of the areas of decalcification—for instance, those in the skull—have remained unchanged. There are signs of healing in some of the diseased areas of the skeletal system. The large defect at the head of the right femur has practically disappeared. The arrest of the disease is also demonstrated by the fact that none of the vertebrae has collapsed, despite the heavy work the man is doing.

Although this man is free from symptoms and has regained 35 pounds, at best the disease was only arrested, because in May 1945, when he felt entirely well, the bone marrow still contained many myeloma cells. The sedimentation rate of the red blood cells has remained high (81 mm. per hour in March 1946).

CASE 2.—Mrs. E. W., 61 years of age, had been suffering from severe pain in the lower part of the back beginning in March 1944. Since May she had been unable to walk and had a great deal of pain even when turning in bed. Between October and December she was in another hospital, where she was confined to bed. At that time roentgenologic examination showed only a moderate degree of osteoporosis. The condition was rapidly progressive, and in February 1945 the patient was admitted to the Mount Sinai Hospital. At this time she could hardly move in bed because of pain on slightest motion. Even slight shaking of the bed caused severe pain.

TABLE 2.—*Results of Treatment of Twelve Patients Having Myeloma With Stilbamidine and Pentamidine*

	Treatment with Stilbamidine		Total Dosage, Mg.	Bence-Jones Protein in Urine	Globulin in Serum, Gm. in Each 100 Cc.	Total Protein in Serum, Gm. in Each 100 Cc.	Formaldehyde Reaction	Results
	Started	Finished						
J. G.	2/18/45	3/20/45	2,500	—	2.7	6.5	—	Excellent
E. W.	4/17/45	5/17/45	1,175	—	1.6	6.2	—	Excellent; relapse July 1946 after 16 months
	6/15/45	7/ 9/45	1,225					
	6/10/46	7/ 7/46	2,800					
	8/ 6/46*	9/ 7/46*	1,000					
	9/10/46	9/26/46	850					
J. M.	2/12/46	3/14/46	2,150	++	1.9	7.1	—	Pain disappeared; died of myeloma in kidney 4/11/46
K. B.	4/ 5/46	6/ 7/46	3,300	++	1.7	8.7	—	Excellent
J. M.	4/27/46	6/19/46	5,175	+	5.6	11.8	++	Pain disappeared; died of thrombopenia 6/8/46
J. B.	4/ 7/46	6/ 8/46	5,550	—	5.3	12.6	+++	Pain disappeared; transverse lesion in cord
A. E.	7/ 2/46	8/ 4/46	4,050	+	2.9	7.2	Doubtful	Pain disappeared
R. V.	7/ 9/46	8/ 4/46	2,250	—	3.4	8.5	Doubtful	Excellent
F. R.	7/ 2/46	9/24/46	6,000	—	3.7	7.5	+++	Excellent
G. E.	6/ 2/46*	6/22/46*	1,300	—	3.6	6.6	+	No result with pentamidine; good result with stilbamidine; died of diabetic coma 9/20/46
	6/22/46	8/ 4/46	4,500		4.0	6.9	..	
H. C.	6/21/46	8/ 2/46	4,350	++	7.7	15.4	++	No result with stilbamidine; excellent result with pentamidine
	8/10/46*	9/24/46*	1,000					
S. C.	6/21/46*	8/ 4/46*	2,200	—	4.1	7.4	+	Excellent result with pentamidine

* On these dates treatment was with pentamidine.

The hemoglobin was 65 per cent. There were 10,200 white blood cells with a normal differential count. The sedimentation rate of the red blood cells was first increased (18 mm. in thirty-seven minutes, Linzenmeyer method) but was later found to be normal (18 mm. in sixty-one minutes) even before the treatment with Stilbamidine was started. During the entire observation, the sedimentation rate has remained normal.

The urine did not contain Bence-Jones protein. The blood serum contained 12 mg. of calcium per hundred cubic centimeters, 4 mg. of inorganic phosphorus and 9 King-Armstrong units of phosphatase. The total proteins in the serum were 6.2 Gm. per hundred cubic centimeters, with 4.6 Gm. of albumin and 1.6 Gm. of globulin. The formaldehyde gel reaction was negative.

Comparison of roentgenograms made in March 1945 with roentgenograms made in October 1944 revealed that the disease had progressed rapidly. The skull now contained numerous small areas of bone destruction. There were several pathologic fractures in the pelvis. Many new osteolytic areas had developed in the arms and legs. Puncture of the sternal marrow and sternal biopsy confirmed the diagnosis of multiple myeloma.

A course of Stilbamidine was given between April 17 and May 17, 1945, totaling 1,175 mg. A second series was given between June 15 and July 9, totaling 1,100 mg. Shortly after the beginning of May the patient could sit up in bed without help. In August, after the second series had been terminated, she returned home, where she resumed her usual activities as a housewife. In August anesthesia of the forehead developed. This gradually spread to the cheeks and the lips, but after a few months it started to recede.

When the patient was readmitted for a new check-up in February 1946, some numbness in the distribution of the second branch of the trigeminal nerve still persisted. Roentgenologic examination showed that none of the osteolytic areas had increased in size. The fractures of the pelvis had healed, and there was considerable recalcification and reconstruction of bone in the upper part of both femurs and in the humeri. In April a third series of injections of Stilbamidine was given, totaling 1,225 mg. In this patient also, clinical recovery only had been achieved. In March aspiration of the iliac crest still revealed the presence of 30 per cent myeloma cells in the bone marrow: evidently the disease had only been arrested, not cured.

At the end of July 1946 a relapse of the multiple myeloma set in, which is now being controlled again by a new series of injections of Stilbamidine.

Case 3.—Mrs. K. B., 47 years old, was admitted with the following history: In August 1944 a lower right molar tooth was extracted and a cyst of the jaw removed. In September she noticed the onset of dull gnawing pain in the right thigh. After November, pain in the lower ribs and in the back developed. The pain became progressively worse, so that in September 1945 she was unable to walk without a stick. She was admitted to another hospital, where a diagnosis of multiple myeloma was made. She then received roentgen treatment (2,400 r and 3,000 r) to the right side of the pelvis and to the right hip without relief of pain. The second series of roentgen treatments was finished in September.

In March 1946 she was transferred to the Mount Sinai Hospital. On admission she could not move in bed without pain. When she tried to lift her head from the pillow she suffered excruciating pains. The skeleton was tender on pressure. The mobility of the right hip was much impaired, and abduction of the right leg was greatly limited.

Hemoglobin was 85 per cent. There were 5,200 white blood cells with 3 per cent plasma cells. With this exception the differential count was normal. The sedimentation rate was 20 mm. per hour (Westergren method). The urine contained a moderate amount of Bence-Jones protein. The blood serum contained 11.1 mg. of calcium per hundred cubic centimeters, 2.5 mg. of inorganic phosphate and 7 King-Armstrong units of phosphatase. The total proteins in the serum were 7.5 Gm. per hundred cubic centimeters, with 4.3 Gm. of albumin and 3.2 Gm. of globulin. The formaldehyde gel reaction was negative.

Roentgenologic examination of skull, long bones, chest and spine showed numerous destructive lesions. Most of the lesions were small, but large osteolytic areas were seen in the right frontal bone, the left radius and both femurs. A large osteolytic area had destroyed about 50 per cent of the head and the neck of the right femur.

Puncture of the sternal marrow showed the presence of numerous plasma cells.

Between April 5 and May 6 seventeen intravenous injections of Stilbamidine were given, totaling 2,250 mg. On April 8, after three injections had been given, the patient noticed pronounced improvement. The pain in the back had diminished so that now she could lift her head without difficulty. On April 15, after 900 mg. of Stilbamidine had been given, the patient stated that "she was incomparably improved." She was now able to sit up in bed unaided without pain in the back or the right hip. After April 25 she was put in a wheelchair daily, where she could sit without discomfort. On May 4 the patient felt rather well. On standing or after sitting in a chair for a long time she noticed some weakness of the muscles of the hips and the thighs, but did not feel pain. The mobility in the right hip was now practically normal.

New roentgenograms of the head of the right femur showed no change in the large destructive lesion. The patient was therefore not permitted to walk. It was decided at this time to give additional roentgen treatment. The pains due to the myelomatous disease were halted by the treatment with Stilbamidine, but it was hoped that roentgen irradiation might now bring about recalcification.

However, even after this course of irradiation no pronounced evidence of recalcification could be found.

The treatment with Stilbamidine was terminated June 4; by this time a total of 3,450 mg. had been given. The patient now walked about freely and painlessly. Only with difficulty could she be persuaded to use a cane. In December, nearly eight months after the termination of treatment, the patient was in excellent general condition and continued to walk around freely. At this time the sedimentation rate of the red blood cells had become completely normal, 5 mm. per hour. The total blood count showed normal values.

COMMENT

For all 15 patients with multiple myeloma treated with Stilbamidine or Pentamidine and kept on a diet low in animal protein, considerable improvement was obtained. These substances evidently have a specific influence on the disease, as is evidenced by the rapid alleviation of pain after the treatment has been instituted. The disease is, however, not cured but is temporarily checked in its development. The latter result can be obtained even in cases in which the disease has been rapidly progressive before the treatment is started.

A word of caution is in order. The disappearance of the pain may lead to premature mobilization of these patients. Despite the alleviation of pain, resulting from the treatment with Stilbamidine, the skeleton is still intensely diseased. Mobilization should therefore be gradual in order to prevent new fractures.

It is pertinent to inquire why the pains disappear although the disease persists. It may be assumed that Stilbamidine, and sometimes also Pentamidine, is capable of arresting proliferation of the myeloma cells because in the cases reported the osteolytic lesions have not expanded for some time after the cessation of treatment with Stilbamidine. There are other conditions in which arrest of abnormal proliferation in bone is accompanied by disappearance of pain even if the disease of the bone persists. In patients with Recklinghausen's disease of the bone, removal of the parathyroid adenoma often relieves the pain in the bone within two days after the operation. At this time the bone is still intensely diseased but the progressive erosion by osteoclastic proliferation is arrested. Analogous conditions may well exist in patients with mammary cancer and skeletal metastases in whom testosterone treatment occasionally relieves the pain. In these cases the carcinomatous deposits in the bone do not disappear but for some time the proliferation is halted. During this period the pain is much relieved. It is therefore possible that arrest of proliferation of the myeloma cells explains the improvement observed in patients treated with Stilbamidine and Pentamidine.

The arresting influence which Stilbamidine seems to exercise on the development of multiple myeloma may well be connected with observations recently reported by Kopac.[8] He found that in tissue cultures Stilbamidine destroys neoplastic cells of transplantable animal tumors without damaging the normal cells. The shape of the nuclei of tumor cells changed under the influence of Stilbamidine, and mitosis of the tumor cells was stopped. Kopac is of the opinion that Stilbamidine has a chemical influence on certain specific nucleoproteins of the nuclei. In the series reported here no change of the nucleoprotein of the nuclei of the myeloma cells could be observed. However, as mentioned earlier, in

8. Kopac, M. J.: Tr. New York Acad. Sc. 8:5, 1945.

10 of 13 patients with myeloma treated with Stilbamidine, specific changes of the nucleoprotein of the cytoplasm, that is, of the ribonucleic acid, occurred.[7] Until now these changes of the cytoplasm of the myeloma cells have not been found after treatment with Pentamidine.

SUMMARY

A series of fifteen or more intravenous injections of 150 mg. of Stilbamidine (4,4-diamidinostilbene), combined with a diet low in animal protein, relieves the pain in most cases of multiple myeloma. For 1 patient the same result was obtained by intramuscular administration of 100 mg. of Pentamidine (4,4'-[pentamethylenedioxy] dibenzamidine). These compounds do not contain antimony. In 1 patient Stilbamidine had no result but Pentamidine relieved the pain. However, the reverse was true in 2 other cases in which Pentamidine seemed to be ineffective but the pain disappeared after treatment with Stilbamidine. Satisfactory even if temporary results have been obtained for all 15 patients with myeloma treated up to the present time.

Improvement starts soon after the inception of the treatment, often beginning after the third or fourth injection. No results have been obtained when the treatment has been accompanied by a diet high in protein.

Fifteen patients have been treated to date. In all cases the pain was favorably influenced. Relapses did occur. Eleven patients were able to walk at the time of discharge from the hospital. One of these died later of diabetic coma. One patient had paraplegia before the treatment was started, and 2 other patients died of myeloma of the kidney and thrombopenia, respectively.

The treatment merely checks the disease and does not cure it. Even when the patients feel completely well, myeloma cells can still be found in the bone marrow and Bence-Jones proteinuria and hyperglobulinemia persist.

During treatment with Stilbamidine specific morphologic changes develop in the cytoplasm of the myeloma cells, consisting of precipitates of ribonucleic acid.

Immunization Against Influenza.—Reactions to influenza vaccine correspond in severity and character to reactions following typhoid vaccine. They are primarily attributable to the virus content. In the studies referred to, about half of the vaccinated individuals had some complaints and about 1 to 2 per cent developed febrile reactions up to 101.5 F. within twenty-four hours of inoculation. Such symptoms usually last no longer than a day. At the site of inoculation, edema, redness and tenderness may develop in about twelve hours and persist for about a day or slightly longer. The local and systemic symptoms are related to the quantity of virus administered rather than to any nonvirus impurities that are present. One word of caution is warranted, and that is the danger of anaphylactic reactions in persons with known egg sensitivity who are given any vaccine of egg origin. The development of sensitivity to repeated inoculations seems to be less of a risk or no risk at all. An adult who has once been given an injection of vaccine originating from an egg, and this includes a good number of vaccines, is much less likely to have an acute reaction than one who is to have his first inoculation. . . . On the basis of the results of these studies carried out by the Commission on Influenza, the Surgeon General directed that plans be made to vaccinate the entire army in the fall of 1945, using vaccine prepared in the same manner as that employed in the field studies. For the first time development of mass production as well as mass immunization with influenza vaccine was involved and was accomplished successfully.—Salk, Jonas E., and Francis, Thomas, Jr.: Immunization Against Influenza, *Annals of Internal Medicine*, September 1946.

PNEUMONIA FOLLOWING NONPENETRATING PULMONARY INJURIES

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"Post-traumatic pneumonia" is a loose term which has been used to describe pneumonia following chest injury, pneumonia following trauma to the body generally,[1] and pneumonia complicating penetrating chest wounds.[2] The phrase post-traumatic pneumonia is used in this paper to indicate the types of pneumonia which follow trauma to the chest. Cases of penetrating wounds are not included because pneumonitis in such cases is usually due to direct contamination.

This report is based on observations made on 73 adult patients with post-traumatic pneumonia treated in this hospital. Every patient had an acute febrile illness with signs and symptoms of pneumonia confirmed by roentgenograms. Patients who were unconscious or who received a general anesthetic are not included in this study. Patients who had emesis were excluded, as were patients with possible aspiration or hypostatic pneumonia. All patients in whom pneumonia developed one week subsequent to their injury were ambulatory, and the cases are reported later.

Twenty-eight patients with post-traumatic pneumonia had an intact thorax; 43 patients had fractured ribs, 1 had a fractured scapula and 1 had a fractured sternum.

Three patients died with a resultant mortality rate of 4.1 per cent.

INCIDENCE

Moritz [3] and Blumer,[4] quoting the German literature, have stated that 0.13 to 4.4 per cent of pneumonia is due to trauma.

In this hospital 73 of 3,170 cases of all types of primary pneumonia were due to trauma, the incidence of post-traumatic pneumonia being 2.3 per cent.

The incidence as to age and sex was similar to that reported from this hospital for primary pneumococcic pneumonia.[5]

PATHOGENESIS OF POST-TRAUMATIC PNEUMONIA

It has long been known that pneumonia may follow simple contusion of the chest wall. Frequently such cases have been regarded with skepticism, since one could not be certain that the patient did not have pneumonia before the injury or that the pneumonia and the injury were not coincidental.[3] As more cases were collected, and as the knowledge of the pathogenesis of pneumonia increased, trauma to the chest has been accepted as an etiologic factor in pneumonia.[6] Austrian [7]

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1. Stoneburner, L. T., and Finland, M.: Pneumococcic Pneumonia Complicating Operations and Trauma: Analysis of Two Hundred and Seventy-Nine Cases of Postoperative and Ninety-Two Cases of Post-Traumatic Pneumonia Associated with Typed Pneumococci, J. A. M. A. **116:** 1497 (April 5) 1941.
2. Litten, cited by Blumer,[4] p. 162.
3. Moritz, A. R.: Pathology of Trauma, Philadelphia, Lea & Febiger, 1942, pp. 183-199.
4. Blumer, G.: Trauma and Pulmonary Disease, in Brahdy, L., and Kalm, S.: Trauma and Disease, Philadelphia, Lea & Febiger, 1941, pp. 159-162.
5. Collen, M. F., and Phillips, E.: Optimum Dosage of Sulfadiazine in the Treatment of Pneumococcic Pneumonia, Arch. Int. Med. **76:** 22 (July) 1945.
6. (*a*) Robertson, O. H.: Newer Knowledge Concerning the Inception of Pneumonia and Its Bearing on Prevention, Ann. Int. Med. **18:** 1 (Jan.) 1943. (*b*) Fallon, M.: Lung Injury in the Intact Thorax with Report of a Case, Brit. J. Surg. **28:** 39 (July) 1940. (*c*) Parker, E. F.: Injuries of the Pleura and Lung, J. South Carolina M. A. **36:** 218 (Aug.) 1940. (*d*) Berry, F. B.: The Treatment of Injuries to the Chest, Am. J. Surg. **54:** 280 (Oct.) 1941. (*e*) Spicer, F. W.: Trauma and Internal Disease, Philadelphia, J. B. Lippincott Company, 1939, pp. 103 and 124-128. (*f*) Stoneburner and Finland.[1] Moritz.[3] Blumer.[4]
7. Austrian, C. R.: Acute Lobar Pneumonia, in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1945, vol. 3, p. 55.

and Shipley,[8] in recent articles, expressed the opinion that there was some doubt that trauma could be an etiologic factor in pneumonia. Shipley stated that "most pathologists and bacteriologists look askance at trauma as an etiologic factor in pneumonia." However, the work of de Takats and his associates,[9] Robertson,[6a] and Coryllos and Birnbaum [10] has made the pathogenesis of post-traumatic pneumonia clear.

Until the work of de Takats, Fenn and Jenkinson [9] appeared, a rational explanation of the pathogenesis of post-traumatic pneumonia in cases without definite clinical evidence of pulmonary contusion was lacking. Blumer [4] thought that the injury probably lowered resistance to infection. Schiff [11] thought that post-traumatic pneumonia was due to vagal stimulation which produced vasodilatation in the pulmonary field.

De Takats, Fenn and Jenkinson [9] demonstrated by animal experiments that blunt injury to the wall of the chest with or without fracture of the ribs produced a spasm of the bronchial tree and bronchial hypersecretion which resulted in pulmonary atelectasis. Bilateral sectioning of the vagi or a sufficient dose of atropine prevented the occurrence of this chain of events. This proved that atelectasis following trauma to the chest was due to a vagal reflex. These authors also cited clinical cases which supported their experimental work. Coryllos and Birnbaum [10] showed that unrelieved atelectasis is followed by pneumonia. Robertson's [6a] experiments proved that local pulmonary irritation or injury is an important factor in the pathogenesis of pneumonia. Pulmonary injury and/or atelectasis is frequently present in patients with nonpenetrating pulmonary injuries.[12]

Moritz [3] stated that the pathology of post-traumatic pneumonia did not differ from that of lobar pneumonia.

PATHOGENESIS AND PATHOLOGY OF PREDISPOSING PULMONARY LESIONS

It has long been known that extensive pulmonary injury may follow trauma which may not mark or damage the thoracic wall. Fallon [6b] stated that Morgagni first described such pulmonary lesions in 1761. Reports of cases have appeared sporadically in the English literature since 1840.

The work of Zuckerman [13] and of Williams [14] established that pressure applied suddenly to the thorax was capable of producing pulmonary injury without damaging the thoracic wall. Any sudden pressure on the thorax in excess of 2½ to 7½ pounds per square inch may result in pulmonary damage, and if the pressure has been applied only momentarily the thorax may not be marked. This is due to the elasticity of the thorax. It has been demonstrated that the sternum of cadavers may be compressed to the vertebral column without fracturing the ribs.[5]

Osborn [15] has calculated that the pressure sustained on the thorax in automobile accidents may greatly exceed 7 pounds per square inch. In 2 of his cases, pressures far in excess of 7 pounds per square inch had been applied to the thorax for 1/30 and 1/45 of a second, respectively. These cases were without fractures or marks on the thorax.

Zuckerman [13] proved in blast injuries that it is the sudden compression of the wall of the chest which contuses the underlying lung. This has been confirmed by Williams,[14] Wilson and Tunbridge [16] and Osborn [15] as the mechanism of pulmonary injury regardless of the source of the force.[17]

Klubs [11] showed in animal experiments that blows delivered to the anterior and lateral aspects of the chest caused more extensive and more numerous injuries to the underlying lung than did blows delivered posteriorly. This is so because the posterior thoracic wall is relatively rigid and thick and is not compressed readily. It is interesting to note that I have not observed a single case of pulmonary injury following strictly posterior blows.

The common causes of lung injuries in the intact thorax are falls from various distances, blows on the chest by flying or falling objects, auto and aviation accidents and "blast." [18] My experience has been similar except that it has not included aviation accidents or "blast" injuries.

There are three types of pulmonary injuries: [15] those due to direct violence, to contrecoup and to "pincer" forces in V-shaped spaces. Lung injuries due to direct violence may show rib markings. These are well seen in children and in animals. The lesion occurring most commonly after direct violence is contusion of the parietal pleura.[19] Klubs [11] also showed that fibrinous pleuritis was common over the affected lobe and demonstrated fine pleural adhesions over the contused areas as early as nine hours after injury. In direct trauma, the lung below the incoming ribs will show varying degrees of subpleural ecchymosis or hematoma and hemorrhagic consolidation of the underlying lung. The latter is due to rupture of the alveolar capillaries.

The typical contrecoup lesion is posterior because the chest is fixed posteriorly and the thorax is compressed from the front and sides. Osborn [15] has elucidated the pathology of these lesions, and this description is based on his work: The earliest contrecoup lesion is a hemorrhagic straight line almost constantly corresponding to the angles of the ribs. This line is often 1 cm. wide and 20 cm. long and usually does not reach to the extreme base but may extend posteriorly to the cupula pleurae. This lesion may be missed easily at autopsy. In addition to the hemorrhagic line, a row of tiny blisters may be present. The hemorrhagic line is due to subpleural hemorrhage and hemorrhagic contusion of the underlying alveoli. Contrecoup lesions may be massive and may endanger life. The lesion may be on the side opposite the direct blow. Extensive contrecoup lesions show hemorrhagic consolidation from the angle of the ribs laterally and anteriorly and may blend with the direct lesion.

The third type of lesion due to "pincer" forces in V-shaped spaces was first described by Osborn [20] in 1940. The V-shaped spaces in the thorax are the costophrenic angles and the posterior part of the right middle lobe. In these spaces pincer forces may be applied to the sides of the V, thus contusing the struc-

8. Shipley, A. M.: Injuries of the Chest, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1945, vol. 4, chap. 10, p. 20.
9. de Takats, G.; Fenn, G. K., and Jenkinson, E. L.: Reflex Pulmonary Atelectasis, J. A. M. A. **120**: 686 (Oct. 31) 1942.
10. Coryllos, P. N., and Birnbaum, G. L.: Syndrome of Pneumococcic Bronchial Obstruction, Arch. Int. Med. **51**: 290 (Feb.) 1933.
11. Cited by Fallon.[6b]
12. Phillips, E.: Non-Penetrating Pulmonary Injuries, Permanente Found. M. Bull. **3**: 97 (July) 1945.
13. Zuckerman, S.: Experimental Study of Blast Injuries to the Lungs, Lancet **2**: 219 (Aug. 24) 1940.
14. Williams, E. R. P.: Blast Effects in Warfare, Brit. J. Surg. **30**: 38 (July) 1942.
15. Osborn, G. R.: Findings in 262 Fatal Accidents, Lancet **2**: 277 (Sept. 4) 1943.
16. Wilson, J. V., and Tunbridge, R. E.: Pathological Findings in a Series of Blast Injuries, Lancet **1**: 257 (Feb. 27) 1943.
17. Problems of Blast Injuries, Brit. M. J. **1**: 94 (Jan. 18) 1941.
18. (*a*) Hass, G. M.: Type of Internal Injuries of Personnel Involved in Aircraft Accidents, J. Aviation Med. **15**: 77 (April) 1944. (*b*) Berry,[6a] Osborn.[15]
19. (*a*) Blumer,[4] chap. 5, p. 145. (*b*) Parker,[6c] Spicer,[6c] Klubs.[11]
20. Osborn, G. R.: Phrenico-Costal Sinus Pneumonia, Brit. M. J. **2**: 317 (Sept. 7) 1940.

tures in the V-space. The contusion in the costophrenic angle is caused by nipping of the lung between the lateral wall of the chest and the spleen or the liver. The posterior part of the middle lobe of the right lung is apt to be nipped between the upper and the lower lobe.

Cavity formation is common in extensive contusions.[15] These are usually seen at the bases. Their walls are smooth and are formed of hard blood clot. Wilson and Tunbridge[16] have described such cavitations in blast injuries. Fallon[6b] reported the case of a 24 year old medical student in whom there developed a hemorrhagic cavity in the lower lobe of the left lung following a blow on the chest sustained while boxing.

Hass[18a] has stated that the subpleural blebs (Osborn's "blisters") are common in aircraft accidents. The blebs are thin walled and occasionally rupture to produce pneumothorax. Deep seated emphysema may also be present, especially in the lower lobes, where the emphysematous areas appear as multiple spherical air-bearing spaces from 2 to 5 mm. in diameter.

PULMONARY INJURIES ASSOCIATED WITH POST-TRAUMATIC PNEUMONIA

In the past three years, 44 adult patients with pulmonary injury with intact thorax have been observed in this hospital. In 4 of these patients with previously normal lungs pneumothorax developed following trauma to the chest, and in 1 of these pneumonia developed. Pneumothorax in the intact thorax following trauma to normal lungs is not as infrequent as the German literature indicates.[19a] Washburn[21] cited such a case and found similar ones in the literature. Roberts and Tubbs[22] reported 3 cases recently.

One patient with hemopneumothorax and 2 patients with hemothorax with intact chest walls were instances of secondary hemothorax. Secondary hemothorax occurs eight to twenty-one days after the injury[19a] and is presumably caused by a rupture of a subpleural hematoma. The patient with hemopneumothorax was an elderly man with a long standing asthma. Pneumonia did not develop in these patients.

Thirteen cases of pulmonary contusion were diagnosed on the basis of hemoptysis and clinical and/or roentgenologic signs of consolidation. In 6 of these patients there later developed pneumonia (table 1). Three additional cases of unsuspected pulmonary contusion with intact thorax were found at autopsy.

Twenty-one patients in whom pneumonia developed after chest injuries without fractures are presumed to have sustained pulmonary injury and/or atelectasis. The rationale for including such cases is based on the work of de Takats and his co-workers cited previously.

Fractures of the thorax are recognized readily but may be missed in cases in which the thorax is not marked. Pulmonary injuries in patients with fractures of the thorax are similar to those already described. In addition, puncture of the lung or its laceration by bone fragments may be present. Seventy-six instances of pulmonary injuries associated with fractures of the chest wall were observed.

Pneumothorax in the presence of fractured ribs usually is presumed to be due to laceration of the lung by a rib fragment but may be due to rupture of a subpleural bleb.[18a] Four cases of pneumothorax were observed. One patient had a tension pneumothorax and subcutaneous emphysema. The presence of subcutaneous emphysema presupposes a laceration in the parietal pleura as well as in the lung.[6c] The patient with tension pneumothorax died fifty hours after the injury. An extensively contused right lung with two small tears in the visceral pleura and a laceration in the parietal pleura were found at autopsy. In 2 other patients with pneumothorax traumatic pneumonia developed (table 1).

Hemopneumothorax must be due to laceration of the lung.[6c] Six such cases were seen. One patient had a stove-in chest, a tension pneumothorax, hemothorax and subcutaneous emphysema; in spite of a complicating pneumonia the patient recovered. In 3 patients pneumonia developed; a fatal case is reported later (case 14). Only one instance of secondary hemopneumothorax was observed in patients with fractured ribs.

Laceration of the lung is followed by slight bleeding which seldom menaces life.[23] Extensive intrathoracic hemorrhage may follow laceration of an intercostal or internal mammary vessel or a vascularized adhesion.[3] Fourteen cases of hemothorax were seen with fractured ribs. One case of secondary hemothorax followed fracture of the clavicle. Three additional cases of secondary hemothorax followed fracture of the ribs. The longest period between injury and the development of hemothorax was twenty-six days.

TABLE 1.—*Traumatic Pulmonary Lesion Present at Onset of Pneumonia*

Lesion Present at Onset of Pneumonia	No. of Patients with Intact Thorax	No. of Patients with Fractures of Thorax
Contusion of lung	6	6
Pneumothorax	1	2
Hemopneumothorax	..	3
Hemothorax	..	4
Mediastinal emphysema	..	1
Subcutaneous emphysema only	..	2
No obvious lesion	21	27
Totals	28	45

When the hemothorax is small it is usually assumed that the bleeding is from a lacerated lung, but the bleeding may be from the parietes. A case of hemothorax due to laceration of the parietal pleura, proved at autopsy, is reported later (case 12).

Six patients with hemothorax also had subcutaneous emphysema, but intrapleural air could not be demonstrated.

In 6 fatal cases of hemothorax wherein death was due to trauma and not to pneumonia, 4 patients had gross laceration of the lung by rib fragments. Two of these patients had a stove-in chest and extensive pulmonary contusion. Three cases of fractured ribs and hemothorax were not recognized ante mortem because extensive injuries of the head or extremities drew attention away from the chest, which was unmarked in each instance.

One patient with hemothorax and fractures of the sternum and third rib on the left side also displayed widening of the mediastinum by roentgenologic examination. After twelve days the mediastinal shadow was normal. This was assumed to have been a mediastinal hemorrhage.

In 4 of the 18 patients with hemothorax, pneumonia developed (table 1). The other surviving patients ran a temperature up to 101 F. until the blood was absorbed or evacuated from the pleural cavity.

21. Washburn, F. H.: Traumatic Pneumothorax Without Gross Injury to the Chest Wall (Case Report), Dis. of Chest **9**: 455 (Sept.) 1943.
22. Roberts, J. E. H., and Tubbs, O. S.: Recent Experience with War Wounds of the Chest, Am. J. Surg. **54**: 289 (Oct.) 1941.

23. Moritz,[3] Parker.[3c]

Eighteen patients with pulmonary contusion and/or laceration without obvious hemothorax and with rib fractures were treated. The diagnosis was made on the basis of hemoptysis and/or signs of pulmonary consolidation in the absence of evidence of pulmonary infection. Six of these patients subsequently had pneumonia (table 1).

Five patients with fractured ribs had subcutaneous emphysema without other clinical or roentgenologic evidence of pulmonary injury. In 2 of these patients pneumonia developed later. Only 1 patient had preexisting pulmonary disease, namely, pulmonary emphysema with large bilateral bullae. A patient with mediastinal and subcutaneous emphysema contracted pneumonia (table 1).

Twenty-seven patients with thoracic fractures did not have definite evidence of pulmonary injury until pneumonia developed. The reasons for including these cases in this report have been discussed previously.

The diagnosis of pulmonary injury is frequently missed. Osborn [15] and Hass [15a] cited cases in which the symptoms were erroneously ascribed to shock or head injury. Dean, Thomas and Allison [24] stated that physical signs of pulmonary injury may be present although the patient lacks symptoms referable to the respiratory system. The diagnosis must first be suspected and then confirmed. Symptoms of shock, anxiety, restlessness, dyspnea and cyanosis may be due to pulmonary injury.[25] The presence of hemoptysis or of any abnormality in the chest should suggest the diagnosis. Unfortunately, it is a frequent practice in cases of contusion of the chest and fractured ribs to strap the chest without examining the lungs.

Every case suggestive of injury to the chest should have frequent, careful physical and roentgenologic studies. Westermark [26] found by careful roentgenologic studies that 65 per cent of patients with chest injuries but without rib fractures had demonstrable changes in the lungs and that 86.6 per cent of those with fractured ribs had demonstrable changes in the lungs! The practice of taking spot films over areas of suspected rib fractures gives little information about the underlying lung and none about the status of the opposite lung or contrecoup injuries. Economy permitting, lateral and posterior-anterior films of the chest should be made in every case.

Table 2.—*Temporal Relationship of Pneumonia to Injury*

Days from Injury to Onset of Pneumonia	Patients with Intact Thorax		Patients with Fracture of Thorax	
	No.	%	No.	%
1	6	21.4	18	40.0
2	6	21.4	12	26.7
3	13	47.9	7	15.7
4	2	6.2	1	2.2
5	..	....	..	....
6	..	....	3	6.6
7	..	....	1	2.2
8	1	3.1	1	2.2
15	..	....	1	2.2
17	..	....	1	2.2
Totals	28	100.0	45	100.0

Table 3.—*Bacteriology of Post-Traumatic Pneumonia*

Organism	No. of Patients with Intact Thorax	No. of Patients with Fractures of Thorax
Undetermined	6	11
Pneumococcic, would not type	8	20
Pneumococcic, types:		
IV	1	1
VI	2	2
IX	1	..
XI	1	1
XII	1	..
XIII	2*	1
XIX	..	1
XXIII	1	1
XXIV	..	1
XXV	2	1
XXVIII	1	..
XXIX	1	1
XXXI	..	1
XXXII	1	..
XXXIII	..	3
Totals	28	45

* Sputum in 1 case also contained a few type IV pneumococci.

24. Dean, D. M.; Thomas, A. R., and Allison, R. S.: Effects of High-Explosive Blast on the Lungs, Lancet **2**: 224 (Aug. 24) 1940.

25. Osborn,[15] Hass.[15a]

THE TEMPORAL RELATIONSHIP OF TRAUMA AND PNEUMONIA

The interval between trauma and the development of pneumonia is variable. Blumer [4] has stated that the general rule is to disregard trauma as a factor if pneumonia develops after six days. Shipley [8] was of the opinion that if the pneumonia comes two to three days after the injury, it may be presumed that trauma is the exciting cause. Fallon [9b] has stated that pneumonia may follow trauma by one to ten days. Stoneburner and Finland [1] and Spicer [6e] accepted some cases of pneumonia occurring more than two weeks after injury as post-traumatic. The bulk of the reported cases occurred within six days after injury. Pneumonia occurring later must be evaluated carefully.

Table 4.—*Relationship of Pneumonia to Site of Injury*

Site of Pneumonia	No. of Patients with Intact Thorax	No. of Patients with Fractures of Thorax
Same side as injury only	24	30
"Contrecoup" side only	1	9
Same side plus "contrecoup" side	3	6
Totals	28	45

In over 92 per cent of the patients in this series pneumonia developed within six days of the injury (table 2).

BACTERIOLOGIC OBSERVATIONS

Sputum typing was done in 56 (or 76.7 per cent) of the cases. Blood cultures were made in most instances, and pleural and empyema fluids were cultured.

Table 3 shows that there were 56 cases of pneumococcic pneumonia. (One case with sputum containing more streptococci than pneumococci is included because there were more than 11 pneumococci per oil immersion field). Of these, only 28 cases (50 per cent) reacted with specific antiserums, types I to XXXIII. In contrast, 62 per cent of the cases of primary pneumococcic pneumonia in this hospital were type-specific.[5] The small incidence of type-specific pneumococcic pneumonia is interpreted as signifying a preponderance of less virulent and higher type (XXXIV to LXXV) pneumococci in the post-traumatic cases. Indeed, the preponderance of the "higher" and less virulent types of organisms is striking. Types I, II, III, V, VII, VIII, IX and XX, which accounted for approximately 50 per cent of the typed primary pneumococcic pneumonia in this hospital,[5] were not found in the post-traumatic cases.

Only 1 case of bacteremia (type XII) was encountered.

26. Westermark, N., cited by de Takats and others.[9]

SITE OF PNEUMONIA IN RELATION TO SITE OF TRAUMA

In 54 patients (74 per cent) pneumonia developed only on the same side as the injury. Nine patients had bilateral pneumonia, that on the contrecoup side being in the lower posterior lung field. In 10 patients pneumonia developed on the contrecoup side only (table 4).

Stoneburner and Finland [1] failed to find an instance of "contrecoup pneumonia" in 29 patients in whom pneumonia developed following injury to the chest. I am unable to account for this difference between the two series, because contrecoup traumatic pulmonary lesions are common.[12]

Pneumonia of the upper lobe followed direct injury to the upper anterior part of the chest, and in 1 case, to the scapula.

INCIDENCE OF PREVIOUS RESPIRATORY DISEASES OR INJURY TO THE LUNGS

Only 7 patients (9.6 per cent) gave a history of respiratory infection present at the time of injury. Six patients had the common cold, and 1 had asthmatic bronchitis.

TABLE 5.—*Extent and Localization of Pneumonia*

Lobes Involved	No. of Patients with Intact Thorax	No. of Patients with Fractures of Thorax
Single lobe:		
Right upper	2	3
Right lower	10	13
Left upper	..	2
Left lower	11	18
Multiple lobes:		
Right upper and middle	1	..
Right lower and left lower	2	7
Right upper, middle and lower	1	..
Right lower, left lower and right upper	..	2
Right middle and lower and left lower	1	..
Totals	28	45

Table 1 shows the existing traumatic pulmonary lesions known to be present when the pneumonia developed.

TYPE OF THERAPY BEFORE THE DEVELOPMENT OF PNEUMONIA

Table 6 shows the type of therapy used in the treatment of thoracic fractures or contusions of the chest before the onset of pneumonia. Twenty-one, or 29 per cent, of the patients had been treated by immobilization of the thorax by adhesive strapping. Three of these patients had complete circular strapping. One patient had a plaster of paris shoulder spica; 1 had a body cast. The patients who had not received previous treatment had relatively mild injuries of the chest.

CLINICAL COURSE

All 73 cases of post-traumatic pneumonia simulated mild to moderately severe primary pneumococcic pneumonia. Leukopenia and the virulent "lower" type pneumococci were not encountered. The incidence of bacteremia and multiple lobe involvement was low. Sputum counts were generally low. The sputum contained 75 or more pneumococci per oil immersion field in only 2 cases, 1 of which was fatal. The latter patient was the only one who showed definite albuminuria (case 12).

The duration of the post-traumatic pneumonia was comparable to that of primary pneumonia. Over 50 per cent of the patients recovered within one week.

In 2 of the 3 fatal cases the patients had hemothorax and other complications: case 12 also involved a traumatic rupture of the pancreas, and in the other case there were multiple fractures (case 14). The third patient died after a rib resection for empyema.

TABLE 6.—*Therapy of Chest Injury Before Onset of Pneumonia*

Therapy	Patients with Intact Thorax		Patients with Fractures of Thorax	
	No.	%	No.	%
Chest strapping, ambulatory	8	28.6	7	15.7
Chest strapping, rest in bed in hospital	1	3.55	5	11.1
Hospitalization and symptomatic treatment	4	14.3	22	48.9
Shoulder spica	..	....	1	2.1
Body cast	1	3.55	..	....
No therapy	14	50.0	10	22.2
Totals	28	100.0	45	100.0

COMPLICATIONS

The complications of post-traumatic pneumonia are listed in table 7. Almost all complications occurred in patients with fractured ribs.

One patient was treated inadequately elsewhere and was admitted to this hospital with empyema. He was treated unsuccessfully with intrathoracic instillations of penicillin but recovered after rib resection. The other patient with empyema died, and the case is reported later (case 13).

The incidence of pleural effusion, 5.5 per cent, is higher than that of primary pneumococcic pneumonia in this hospital.[5]

TREATMENT

1. *Prophylactic.*—Post-traumatic pneumonia can be prevented or minimized by the early treatment of all patients with injury to the chest for pulmonary atelectasis and potential infection.

De Takats and his associates [9] showed that the intravenous administration of $\frac{1}{150}$ grain (0.0004 Gm.) of atropine sulfate and ½ grain (0.03 Gm.) papaverine hydrochloride will inhibit or break the vagal reflex which causes bronchospasm and hypersecretion. All patients with chest injury should receive such medication early in order to prevent reflex atelectasis. As much as $\frac{1}{60}$ grain (0.001 Gm.) of atropine [27] and 1½ grains (0.1 Gm.) of papaverine [28] can be given intravenously every four hours without untoward effect. The intravenous administration of $\frac{1}{150}$ grain (0.0004 Gm.) of atropine and of ½ grain (0.03 Gm.) of papaverine every four hours for two days after injury will relieve bronchospasm and hypersecretion and combat atelectasis and pulmonary edema.[27] Patients who are not

TABLE 7.—*Complicating Conditions in Seventy-Three Cases of Post-Traumatic Pneumonia*

Complication	No. of Patients with Intact Thorax	No. of Patients with Fractures of Thorax	Total	Incidence, %
Empyema	1	1	2	2.7
Sterile effusion	..	4	4	5.5
Spread to other lobes	..	4	4	5.5
Atelectasis of a lobe	1	2	3	4.1
Pulmonary edema	..	1	1	1.4

27. de Takats, G.; Beck, W. C., and Fenn, G. K.: Pulmonary Embolism: An Experimental and Clinical Study, Surgery **6**: 339 (Sept.) 1939.
28. Phillips, E., and Levine, E. B.: Unpublished data.

hospitalized may be given comparable oral doses of the drugs, although the value of such treatment is not established.

All patients hospitalized with injuries to the chest must receive large doses of penicillin or sulfadiazine early in order to prevent pneumonia. In this series pneumonia developed in 2 patients with blood sulfadiazine levels of less than 8 mg. per hundred cubic centimeters. In patients with higher sulfadiazine blood levels pneumonia did not develop. Penicillin is the drug of choice because of its efficacy and freedom from serious toxic reactions.

Twenty-six consecutive patients with severe chest and pulmonary injuries who were placed on the above regimen did not contract pneumonia or other complicating infections.

2. Active Treatment.—Patients with mild to moderately severe post-traumatic pneumonia responded well to penicillin therapy. Penicillin in doses of 25,000 units should be administered intramuscularly every three hours until the temperature has been normal for forty-eight to seventy-two hours.[29] The oral administration every three hours of 100,000 units of calcium penicillin combined with 2 Gm. of calcium carbonate[30] produced satisfactory therapeutic results in patients with mild pneumonia.

Fig. 1 (case 3).—Type IV pneumococcic pneumonia of the right lung.

Fig. 2 (case 3).—Type IV pneumococcic pneumonia of the right lung.

Patients with severe pneumonia (although rare in the post-traumatic group) should be treated with both penicillin and sulfadiazine. Since it has been demonstrated that "double doses" of sulfadiazine resulted in a decrease in the mortality rate and a decrease in the incidence of complicating conditions without any increase in the incidence of toxic reactions,[5] 5 Gm. of sodium sulfadiazine in 500 cc. of sodium *r*-lactate one-sixth molar were given intravenously, and 5 Gm. of sulfadiazine were given orally (total 10 Gm.) as an initial dose. This was followed by 4 Gm. of sulfadiazine every six hours orally as a maintenance dose until the temperature remained normal for twenty-four hours. Adequate alkali (sodium bicarbonate, potassium bicarbonate or sodium lactate) was used routinely to keep the p_H of the urine at 7.5.

Combined penicillin-sulfadiazine therapy is indicated when there is failure to respond to penicillin alone, leukopenia, high pneumococci count in the sputum, pulmonary edema, shock, toxic delirium or other evidence of severe infection or toxicity. In such cases the dose of penicillin may also be increased up to 50,000 units every two hours.

In this series 2 of the patients who died were treated with sulfadiazine alone and probably would have been saved if penicillin had been available.

Oxygen by inhalation is indicated for cyanosis or severe dyspnea. Other adjuvant therapy such as cough mixtures, fluids and non-narcotic analgesics were used as needed.

3. Relief of Chest Pain.—De Takats[9] and Harmon[31] have emphasized that the treatment of fractured ribs by adhesive strapping is unphysiologic. The use of strapping or of other procedures which cause hypoventilation should be abandoned. Complete circular strapping is never justified.[22] Harmon, Baker and Kornegay[31] have demonstrated that the injection of local anesthetic drugs at the fracture sites relieves pain, enables the patient to cough with relative comfort and increases his vital capacity. These workers inject each fracture site with 2 to 6 cc. of a solution containing 0.5 per cent procaine hydrochloride and 0.1 per cent Eucupine dihydrochloride. (Eucupine is isoamylhydrocupreine.) Sedatives and depressant analgesics are unnecessary except in the treatment of delirium. In such cases meperidine hydrochloride (Demerol hydrochloride) should be used in preference to morphine or codeine to avoid respiratory depression. Relief of pleuritic pain can be obtained by cutaneous anesthesia with ethyl chloride spray or procaine injections as recommended by Dybdahl.[32] In my experience these measures have proved highly efficacious.

4. General Measures.—Patients with pulmonary and chest injuries should be given little, if any, sedatives in order to preserve the cough reflex. Oxygen by inhalation is indicated for cyanosis and dyspnea. Deep breathing exercises or carbon dioxide whiffs may be used for hyperventilation. Expectorants, such as ammonium chloride and saturated solution of potassium iodide to attenuate bronchial secretions, should be given to all patients with thick or tenacious mucus and probably should be used routinely. Frequent movement of bed patients and early ambulation is essential to prevent hypostatic pneumonia.

Patients hospitalized for chest or pulmonary injuries should be in private rooms. All attendants and visitors with respiratory infections should be excluded.[14]

5. Treatment of Associated Conditions.—Shock, hemorrhage and respiratory obstruction received first attention in pulmonary injuries. Patients with shock should be treated with oxygen by inhalation,[33] adequate doses of meperidine hydrochloride to alleviate pain and fear, and plasma or blood transfusions. Fluids should be given with caution in order to avoid acute pulmonary

29. Collen, M. F., and Sellers, A. L.: Penicillin Therapy in Pneumococcic Pneumonia, Permanente Found. M. Bull. **3**: 49 (April) 1945. Collen, M. F.; Sellers, A. L., and Kast, E. C.: Combined Penicillin and Sulfadiazine Therapy in Pneumococcic Pneumonia, Am. J. M. Sc. **211**: 299 (March) 1946.

30. Collen, M. F., and others: Oral Administration of Penicillin, Permanente Found. M. Bull. **3**: 155 (Oct.) 1945.

31. Harmon, P. H.; Baker, L. R., and Kornegay, R. D.: Uncomplicated Fractures of Ribs and Major Injuries of the Chest Wall, J. A. M. A. **118**: 30 (Jan. 3) 1942.

32. Dybdahl, G. L.: Control of Pleuritic Pain by Use of Cutaneous Anesthesia, Permanente Found. M. Bull. **2**: 30 (Jan.) 1944.

edema.[15] It is therefore better to use concentrated plasma or albumin preparations in cases without loss of blood.[34] Patients with pulmonary edema must not be given intravenous fluids, but should be treated with morphine, oxygen by inhalation under positive pressure [33] and intravenous theophylline ethylenediamine. Venesection may be a life-saving procedure in some cases of pulmonary edema.[34]

Hemorrhage in closed hemothorax is seldom alarming,[23] but if signs of bleeding or pulmonary tamponade become alarming, an open operation to ligate a torn vessel is imperative.[22] The current literature recommends the aspiration of hemothorax and partial replacement with air within thirty-six to forty-eight hours after injury.[35] Early aspiration was performed only twice in my series. Patients not treated in this manner had moderate fever which persisted for from five to seven days, or until the pleural cavity was aspirated.

Respiratory obstruction or massive collapse should be treated by aspiration of the mucous plug from the bronchial tree. Bronchoscopy may be a life-saving procedure. Tracheobronchial catheter suction is useful for the removal of accumulated tracheobronchial secretions.

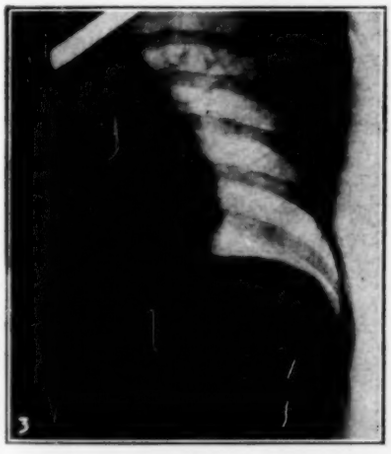

Fig. 3 (case 5).—Fracture of the eighth and ninth ribs on the left side in the midaxillary line.

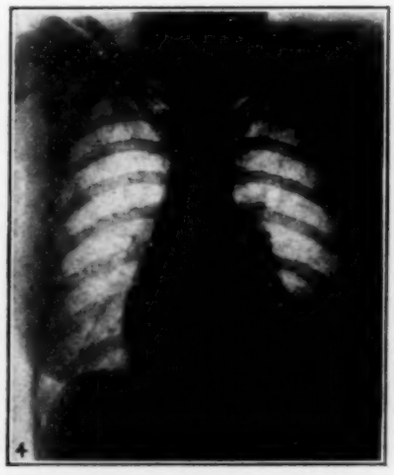

Fig. 4 (case 5).—"Contrecoup" pneumonia, lower lobe of the right lung.

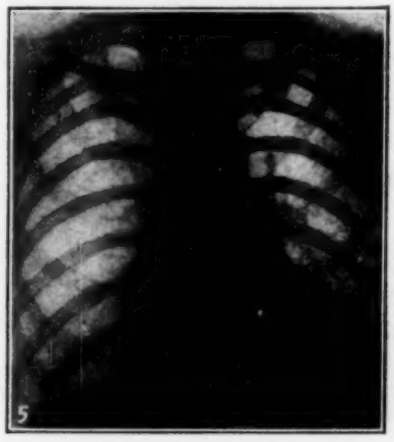

Fig. 5 (case 7).—Fracture of fourth to sixth ribs on the right side complicated by pneumothorax (right) and atelectasis (lower lobe, left).

Tension pneumothorax needs immediate aspiration and does not brook delay. Simple pneumothorax is treated conservatively. Subcutaneous emphysema does not require therapy unless the skin becomes dangerously tight or there is interference with the circulation. Multiple "pie-crusting" incisions are then indicated.

Stove-in chest with paradoxic respiration should be supported by adhesive strapping, sandbags, skeletal traction or skeletal fixation by wiring,[36] if necessary, in order to correct paradoxic respiration and increase the vital capacity.

6. *Treatment of Complications.*—Sterile pleural effusion does not need treatment unless it produces respiratory or circulatory embarrassment. The withdrawal of 1 liter of fluid by thoracentesis is safe. Larger amounts of fluids should be removed only with caution. Empyema may be treated with aspiration followed by intrathoracic instillation of 50,000 units of penicillin[37] once or twice a day. In this hospital, not a frank case of empyema was cured in this manner.[38] When the empyema fluid becomes thick, thoracotomy is indicated. Intrathoracic instillations of penicillin may be of value in aborting empyema in cases of sterile pleural exudates which contain abundant pus cells.

Pulmonary atelectasis can be relieved by the use of expectorants, inhalations of carbon dioxide and forced coughing on the part of the patient. Pulmonary edema complicating pneumonia can be successfully combated by the inhalation of oxygen under positive pressure and the intravenous injection of 0.5 Gm. of theophylline ethylenediamine, 50 cc. of 50 per cent sucrose solution and 250 to 500 cc. of plasma.[39] These may be injected every three hours as necessary.

Spread of the pneumonia to other lobes is an indication for intensive combined therapy with penicillin and sulfadiazine.

REPORT OF CASES

CASE 1.—*Typical Post-Traumatic Pneumonia With Intact and Unmarked Thorax.*—M. G., a white man aged 59, fell 8 feet onto the left side of his chest and left shoulder. The examination was negative except for the patient's subjective complaint of mild pain in the shoulder and chest. The only treatment advised was acetylsalicylic acid. Two days later the patient had a sudden onset of pleuritic pain in the left side, followed by a cough productive of bloody mucopurulent sputum. Physical and roentgenologic examinations revealed pneumonia in the lower lobe of the left lung. The sputum contained many type XXIX pneumococci. Treatment with sulfadiazine resulted in recovery in five days.

CASE 2.—*Development of Post-Traumatic Pneumonia in a Patient with Preexisting Pulmonary Disease Who Was Treated for a Chest Contusion by Adhesive Strapping.*—R. C., a white man aged 46, who had chronic asthmatic bronchitis of five years' duration, slipped and fell to the street and sustained a contusion of the left side of the chest. He complained immediately of pleuritic pain. The chest was strapped. Three days later he entered the hospital with type XI pneumococcic pneumonia in the lower lobe of the left lung. Recovery was uneventful after treatment with sulfadiazine.

CASE 3.—*Multiple-Lobe Pneumonia Following a Severe Blow Which Left the Thorax Unmarked.*—W. S., a white man aged 55, was struck across the anterior right side of the chest

34. Hadfield, G., and Christie, R. V.: A Case of Pulmonary Concussion ("Blast") Due to High Explosive, Brit. M. J. **1**: 77 (Jan. 18) 1941.

33. Barach, A. L.: Principles and Practices of Inhalational Therapy, Philadelphia, J. B. Lippincott Company, 1944, pp. 50-52, 75-79 and 195-197.

35. Traumatic Hemothorax, editorial, Lancet **1**: 315 (March 4) 1944. Berry.[24] Roberts and Tubbs.[22]

36. Henley, R. B.: Personal communication to the author.

37. Brown, B.; Ory, E. M.; Meads, M., and Finland, M.: Penicillin Treatment of Empyema: Report of Twenty-Four Cases and Review of the Literature, Ann. Int. Med. **24**: 343 (March) 1946.

38. Collen, M. F.: Personal communication to the author.

39. Collen, M. F., and Dybdahl, G. L.: The Management of Pneumonia, Permanente Found. M. Bull. **1**: 14 (July) 1943.

by a pipe weighing more than 10 pounds. He was stunned and dyspneic for a short time only. Treatment was not given. Three days later a type IV pneumococcic pneumonia of the right lung developed (figs. 1 and 2). Recovery was uneventful after treatment with sulfadiazine.

CASE 4.—*Pneumonia Following Injury by Eight Days in a Patient Treated With Codeine.*—H. P., a white man aged 35, fell off a ship into the San Francisco Bay. He was rescued immediately. His only complaint was pain in the left side of the chest. Codeine, 1 grain (0.06 Gm.) every four hours, was prescribed. The patient remained ambulatory but took the codeine continually until pneumonia developed in the lower lobe of the left lung on the eighth day. The sputum contained a moderate number of pneumococci which did not type. Recovery was uneventful after treatment with sulfadiazine.

CASE 5.—*"Contrecoup" Pneumonia Which Followed Trauma by Seventeen Days. Previous Treatment by Complete Circular Adhesive Strapping.*—M. W., a white woman aged 31, fell in her home and sustained fractures of the left eighth and ninth ribs in the midaxillary line (fig. 3). The lower chest was completely encircled with adhesive strapping. Seventeen days later pneumonia developed in the right lower lobe (fig. 4). The sputum contained a moderate number of pneumococci which did not type. The patient stated that she had continual chest pain after the injury and that the chest strapping made it "impossible" for her to breathe.

CASE 6.—*"Contrecoup" Pneumonia Following Trauma by Eight Days. Previous Treatment by Complete Circular Adhesive Strapping. Respiratory Infection at the Time of Injury.*—J. M., a white man aged 48, bumped the right side of his chest while working. He had continual pain in the right side for two days. His chest was then completely encircled from the nipple level down with adhesive tape. This relieved his symptoms, but six days later type XXXIII pneumococcic pneumonia developed in the lower lobe of the left lung. Recovery was uneventful.

CASE 7.—*"Contrecoup" Pneumonia in a Patient with Pulmonary Contusion and Atelectasis.*—H. M., a white woman aged 34, was struck in the right upper side of her chest by a vehicle, sustaining fractures of the fourth to the sixth rib on the right side posteriorly near the spine. This was complicated by a pneumothorax on the right and an atelectasis of the lower lobe of the left lung (fig. 5). The chest was strapped, and no specific attempt was made to relieve the atelectasis. The next day signs and symptoms of pneumonia were present in the lower lobe on the left side. The sputum did not type out pneumococci. Recovery was uneventful after treatment with sulfadiazine.

CASE 8.—*Another Case Which Demonstrated the Danger of Chest Strapping in the Presence of Pulmonary Injury.*—C. B., a white man aged 51, fell into a hole 5 feet deep, sustaining fractures of the seventh to the tenth rib on the left side in the axilla. The chest was strapped. The next day the patient complained of bloody sputum and increased pain in the chest. Examination revealed a friction rub and crepitant rales in the base of the left lung. Two days later the patient had findings of bilateral basal pneumococcic pneumonia (fig. 6).

CASE 9.—*Pneumonia Following Injury by Thirteen Days in a Patient Treated With Adhesive Strapping.*—C. K., a white man aged 57, slipped and struck the ground with the right side of his chest, sustaining fractures of the fifth to the ninth rib on the right side in the posterior axillary line. The chest was strapped. The patient had continual pain and complained that he was unable to breathe deeply. Thirteen days after injury pneumococcic pneumonia in the lower lobe of the right lung developed (fig. 7). Recovery was uneventful.

CASE 10.—*Pneumonia Following Fracture of Ribs Treated by Complete Encirclement of the Chest With Adhesive Tape in the Presence of Pulmonary Findings.*—W. D., a white man aged 56, fell 6 feet and struck the left side of his chest with a piece of lumber, sustaining fractures of the fifth to the tenth rib on the left side in the posterior axillary line. On examination of the chest, wheezes were found throughout the lung fields. A history of any previous respiratory symptoms was not obtained. Nevertheless, the lower chest was completely encircled with adhesive strapping. The next day the patient had pneumococcic pneumonia in the lower lobe of the left lung. Sulfadiazine therapy was instituted. Several days later the infection spread to the lower lobe of the right lung. The highest sulfadiazine blood level was 8 mg. per hundred cubic centimeters. A sterile pleural effusion developed, but the patient made a complete recovery after treatment with penicillin.

Fig. 6 (case 8).—Bilateral basal pneumococcic pneumonia.

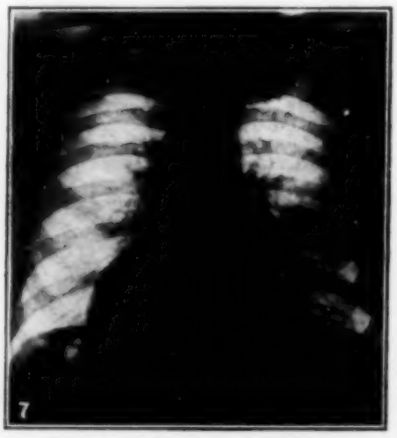

Fig. 7 (case 9).—Pneumococcic pneumonia, lower lobe of the right lung.

Fig. 8 (case 13).—Bilateral pneumonia on the eleventh hospital day after patient was struck by a crane.

CASE 11.—*Pneumonia Developing in the Presence of a Sulfadiazine Blood Level of Six Milligrams per Hundred Cubic Centimeters.*—G. N., a white man aged 56, fell 40 feet, sustaining a stove-in chest on the right side. Sulfadiazine was administered. Two days later pneumonia developed in the lower lobe of the right lung. The blood sulfadiazine level was 6.0 mg. per hundred cubic centimeters at the time. The sputum showed a few pneumococci which did not type. The pneumonia quickly spread to involve four lobes. Penicillin therapy was instituted, and the patient recovered in ten days, in spite of pulmonary edema on the fifth hospital day.

CASE 12.—*Fatal Case of Pneumonia Complicated by a Ruptured Pancreas, Hemothorax and Laceration of the Parietal Pleura.*—L. L., a white man aged 45, was struck by a truck. The seventh, ninth and tenth ribs on the left side were fractured posteriorly. The patient was hospitalized and appeared to be in good condition except for abdominal distention. Three days later the patient became febrile, and it was apparent that he had bilateral pneumonia. The sputum was "loaded" with pneumococci which did not type. The leukocyte count was 36,750 per cubic millimeter with 91 per cent neutrophils. Urinalysis, which had been negative previously, showed 3 plus albumin and many casts. The patient died the next day, in spite of treatment with

sulfadiazine. An autopsy revealed bilateral bronchopneumonia. The left pleural cavity contained 500 cc. of blood. The lungs were intact, but there was a laceration in the parietal pleura on the left. The pancreas was ruptured but intra-abdominal signs of acute hemorrhagic pancreatitis were not present.

CASE 13.—*Fatal Case of Post-Traumatic Pneumonia Complicated by Empyema.*—J. C., a white man aged 56, was struck across the anterior portion of the chest by a crane. He lost consciousness momentarily. Examination revealed evidence of injury to the head and chest. There was an area of ecchymosis under the left clavicle, and rales were present throughout the lung fields. Two days later a pleural friction rub was heard at the base of the right lung, and sulfadiazine was administered. The temperature remained around 100 F. A roentgenogram on the eleventh hospital day revealed a bilateral pneumonia (fig. 8). The sputum contained few pneumococci, but Mycobacterium tuberculosis was not found. A thoracentesis on the nineteenth hospital day revealed early empyema on the right which was treated with penicillin instillations for six days without avail. A resection of the ninth rib on the right side was done on the twenty-fifth hospital day. The empyema fluid removed at surgery grew Escherichia coli in pure culture. Five days postoperatively there was some hemorrhage from the wound, but this was controlled by packing. The next day the patient suddenly became restless and irrational and died. A coroner's autopsy was incomplete, and therefore the cause of death could not be established.

CASE 14.—*Fatal Case of Pneumonia Complicating Hemothorax.*—J. K., a white man aged 57, was struck by a train. He was not unconscious. His left humerus was fractured, and on the left side all the ribs from the fourth down were fractured. Subcutaneous emphysema was present bilaterally over the anterior portion of the chest. A roentgenogram showed a left hemothorax. This was aspirated later. On the second day pneumonia developed in the lower lobe of the left lung. One week later the pneumonia spread to the lower lobe of the right lung, and after an apparent recovery it relapsed. The patient died on the fifty-fourth hospital day. A coroner's autopsy revealed bilateral pneumonia and a healing laceration of the lower lobe of the left lung. The parietal pleura was intact.

SUMMARY AND CONCLUSIONS

In 73 cases of pneumonia following nonpenetrating injuries to the chest, 28 patients had an intact thorax and 45 had fractures of the thoracic cage.

Of the cases of primary pneumonia observed in this hospital, 2.4 per cent were post-traumatic. Over 92 per cent of the cases occurred within six days of the injury.

In 54 patients, pneumonia developed at the site of the direct trauma only.

In 19 patients pneumonia developed at the site of the "contrecoup" pulmonary injury; 9 of the 19 also had pneumonia at the site of the direct trauma.

The course and complications of post-traumatic pneumonia simulate those of mild to moderately severe primary pneumococcic pneumonia. The "higher type" pneumococci are the etiologic organisms usually found in post-traumatic pneumonia.

In consideration of the pathogenesis of pulmonary injury and post-traumatic pneumonia and the errors commonly made in the treatment of chest injuries which facilitate the development of pneumonia, it may be stated that the prophylaxis of post-traumatic pneumonia depends on: (1) the prevention of reflex pulmonary atelectasis, (2) the restoration of normal vital capacity, (3) the attenuation of thick, tenacious bronchial mucus, (4) protection of the patient from respiratory pathogens harbored by others, and (5) prophylactic chemotherapy with adequate doses of penicillin or sulfadiazine.

SIMPLIFIED METHOD FOR CALCULATING DIABETIC DIETS

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and
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Numerous methods have been evolved for the calculation of diets to be used by patients with diabetes mellitus and for the simplified instruction of patients in the use of such diets. Some of these methods involve calculations which are unnecessarily accurate in view of the variable composition of foods, as affected by such factors as the variety of seed, the soil, climatic conditions and harvesting, storage and cooking methods. The fairly common practice of instructing patients to weigh diets can be criticized for the same reason plus the fact that a patient who is "tied to a pair of scales" has much less chance of living a normal life, which is so important from a psychologic point of view. The subject of the percentage of carbohydrate in foods, particularly vegetables, has also been confusing to the patient. In general, we have found that many patients disregarded it and ate whatever vegetable was prepared for them

TABLE 1.—*Food Equivalents*

List 1.—Protein Equivalents—Negligible Carbohydrate, 7 Gm. Protein, 5 Gm. Fat

Meat, fish, poultry—1 oz. (28 Gm.)	Sardines—3 medium
Egg—1	Salmon, tuna, crabmeat—¼ cup
Cheese, American—1 oz. (28 Gm.)	Peanut butter—1½ tbs.
Cheese, cottage—2 tbs.	"Cold meat"—3 thin slices
Oysters, clams, shrimp—5	Frankfurt—1 average size

List 2.—Vegetables—Negligible Carbohydrate, Protein and Fat

Celery	Cucumber	Lettuce	Radishes

List 3.—Vegetables—7 Gm. Carbohydrate, 2 Gm. Protein, Negligible Fat (1 Serving = ½ Cup)

Asparagus	"Greens": beet,	Turnip
Beans, string	chard, dandelion,	Onions
Beets	mustard, kale,	Squash
Broccoli	spinach,	Tomato
Cabbage	turnip	
Carrots		

List 4.—Fruits—10 Gm. Carbohydrate, Negligible Protein and Negligible Fat

Apple—½ medium	Orange—1 medium or ½ cup juice
Applesauce, unsweetened—½ cup, scant	Peach—1 medium
Banana—½ small	Pear—½ large
Berries: raspberries, blueberries or blackberries—½ cup	Pineapple, fresh, diced—½ cup
Cantaloupe—½ medium	Pineapple juice, unsweetened—½ cup
Cherries—12 small	Plums—2 medium
Dates—2 small	Prunes—2 medium
Grapefruit—½ medium	Strawberries—12 large
Grapefruit juice, unsweetened—½ cup	Tangerine—1 large
Grapes—15 medium	Watermelon—1 small slice with rind, ½ lb. (151 Gm.)

List 5.—Carbohydrate Equivalents—16 Gm. Carbohydrate, 3 Gm. Protein, Negligible Fat

Beans, baked and lima—¼ cup	Peas—½ cup, scant
Bread, baker's—1 slice	Potato, white—1 small (size 5 to 1 lb., 454 Gm.)
Corn—¼ cup (1 small ear)	Cereals, cooked—½ cup
Rice, macaroni, noodles—½ cup	Cereals, dry, flakes—1 cup
Graham crackers—2	
Soda crackers—5	

List 6.—Fat Equivalents—Negligible Carbohydrate, Negligible Protein, 4 Gm. Fat

Butter or fortified oleomargarine—1 tsp.
Cream, light—2 tbs.
Mayonnaise—1 tsp.
Oil—1 tsp.
Bacon—1 slice, long, crisp
Milk—(1 cup, 8 oz.) 12 Gm. carbohydrate, 8 Gm. protein, 10 Gm. fat

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at home, irrespective of its carbohydrate content. This practice seldom accounts for more than a 5 to 10 per cent variation in the total carbohydrate intake for the day. Certainly most diabetic patients can tolerate that much variation in their carbohydrate intake.

Many methods of dietary instruction are impractical and unrealistic because they do not take into consideration the patient's food habits. Race, religion and economic status, together with other social and psychologic factors, fundamentally affect the daily selection of food. A laborer who takes his lunch from home presents one problem. His noon meal must be planned around the nonperishable, easily packaged foods. A person with a limited income may not be able to afford more than one serving of fruit and vegetables a day; therefore the carbohydrate in the diet should be figured from less expensive sources. An Italian patient is accustomed to using oil, "pastas," tomato sauces and salads and has definite food patterns. Thus we see that a diet adapted to individual food habits will have a much better chance of being eaten in its entirety.

TABLE 2.—*Summary of Composition of Food Equivalent Groups*

Foods and Equivalents	Carbohydrate	Protein	Fat
Milk—1 cup	12	8	10
Protein equivalents—list 1	0	7	5
Vegetables—list 2	0	0	0
Vegetables—list 3	7	2	0
Fruits—list 4	10	0	0
Carbohydrate equivalent—list 5	16	3	0
Fat equivalents—list 6	0	0	4

Another criticism of some of the diet plans in general use is that they may not contain adequate amounts of the essential nutrients, especially minerals and vitamins. For example, if the amount of milk allowed in the diet is appreciably limited, as it sometimes is because it is a source of carbohydrate, the diet becomes low in calcium and riboflavin. If breads and cereals are greatly restricted in amount, the diet may be low in thiamine. The consumption of gluten bread in the past has also been responsible for a lack of several elements of the B vitamin complex in the diet. The use of whole grain products or of bread and cereals made from enriched flour will tend to prevent this situation. With insulin therapy most diets may contain at least six servings of breads or cereals, which together with average amounts of the other basic foods will supply a normal intake of the vitamin B complex for the usual patient. The sample diabetic diet shown in table 3 illustrates the manner in which such a diet can be adequate nutritionally if it is planned around the basic food groups.

With these factors in mind, we have worked out a simple and useful method of dietary calculations that will result in a diet nutritionally adequate and practical for the patient. This short method has been devised primarily for the busy practitioner who does not have available the hospital or clinic facilities of a trained nutritionist; however, we have found it of equal value to the latter.

TABLE 3.—*Composition of a Diabetic Diet*

Carbohydrate 170 Gm., protein 80 Gm., fat 70 Gm., calories 1,600.

Food	Amount	Protein, Gm.	Calcium, Gm.	Iron, Mg.	Vitamin A, Int. U.	Thiamine, Mg.	Riboflavin, Mg.	Niacin, Mg.	Ascorbic Acid, Mg.
Milk	1 pt. (473 cc.)	16	0.60	0.4	800	0.20	0.84	0.5	..
Egg	1	7	0.03	1.3	500	0.07	0.18	0.6	..
Meat, fish, poultry	5 oz. (141 Gm.)	35	0.03	5.5	...	0.42	0.25	7.5	..
Vegetable:									
Green or yellow	½ cup	2	0.03	1.1	4,000	0.06	0.10	0.4	8
Other	½ cup	2	0.02	0.6	200	0.06	0.05	0.2	5
Fruit:									
Citrus	1	..	0.02	0.4	200	0.05	0.05	0.3	45
Other	1	..	0.02	0.6	400	0.05	0.05	0.7	8
Potato	1 small	2	0.01	0.6	...	0.08	0.02	0.7	5
Bread or cereal, whole grain or enriched	6 sl.	18	0.06	3.0	...	0.36	0.24	3.6	..
Butter or oleomargarine	2 tbs.	..	....	...	900	....	....	...	..
Total		82	0.82	13.5	7,000	1.35	1.78	14.5	71
National Research Council allowances for woman, moderate activity		60	0.80	12.0	5,000	1.20	1.60	12.0	70

TABLE 4.—*How to Calculate a Diabetic Diet Order*

Carbohydrate (C) 180 Gm., protein (P) 80 Gm., fat (F) 60 Gm., calories 1,600

	Amount	C, Gm.	P, Gm.	F, Gm.
Milk, whole	2 cups	24	16	20
Protein equivalents (list 1)	6 serv.	..	42	30
Vegetables (list 2)	As desired	..	..	..
Vegetables (list 3)	2 serv.	14	4	..
1 serv. green or yellow				
Fruit (list 4)	3 serv.	30	..	..
1 serv. citrus				
		68	62	50
Carbohydrate equivalents (list 5) whole grain or enriched	7 serv.	112	21	..
Fat or equivalents	3 serv.	..	..	12
		180	83	62

It is first necessary to have a simplified list of food equivalents; that is, common foods which furnish approximately the same amount of carbohydrate, protein and fat. This is given in table 1. More complete tables of food equivalents are to be found in any textbook of applied nutrition or dietetics. List 1 of this table gives the protein equivalents or foods which have approximately the same composition as 1 ounce (28 Gm.) of meat. We have taken as the average figure for these protein equivalents: carbohydrate—zero; protein—7 Gm.; fat—5 Gm. Vegetables vary in carbohydrate composition and have been classified by some authors as 3, 6 and 9 per cent or 5 and 10 per cent, according to the approximate amount of carbohydrate which they contain. To simplify this classification we have grouped together the raw vegetables which may be eaten in more or less unlimited quantity (list 2) since they contain negligible amounts of carbohydrate. The vegetables of the highest carbohydrate content, such as legumes, corn and potatoes, are included in the

equivalents with bread and cereals in list 5. The rest of the vegetables are grouped together in list 3, and a serving of these vegetables, or one-half cup, is figured as 7 Gm. of carbohydrate and 2 Gm. of protein. These figures represent average values as determined by actual composition and weighted according to the frequency

TABLE 5.—*Number of Servings of Carbohydrate or Fat Equivalents to Complete the Diet Prescription*

180 Gm. carbohydrate in prescription
68 Gm. carbohydrate in diet from sources other than bread or equivalent

16 | 112 Gm.

7 servings of carbohydrate equivalents to fill prescription

60 Gm. fat in prescription
50 Gm. fat from sources other than butter

4 | 10 Gm.

2½ or 3 tsp. of fat equivalents to fill prescription

with which the foods are consumed. For example, over a period of one year patients were questioned in the Diabetic Clinic of the Outdoor Department, Peter Bent Brigham Hospital, regarding the types of vegetables they ate on the preceding day. Five hundred sixty-two reported eating a "5 per cent" vegetable and 482 a "10 per cent" vegetable. Thus, these observations help to substantiate the validity of using a value of 7 Gm. of carbohydrate per serving of these vegetables. Fresh fruits range considerably in their carbohydrate composition. Therefore, for uniformity the servings of fruits in list 4 are converted into amounts which yield approximately 10 Gm. of carbohydrate. List 5 consists of the carbohydrate equivalents. These foods have the same composition as one slice of (baker's) bread which has a value of 16 Gm. of carbohydrate and 3 Gm. of protein. Fat equivalents are given in list 6 and are equal to 1 teaspoon of butter containing 4 Gm. of fat. Since the composition of milk differs considerably from that of other foods, it is placed in a separate category. Moreover, it supplies many of the essential nutrients to the diet and, therefore, it is considered basic in the diet and should be included each day.

TABLE 6.—*Sample Day's Menu*

The carbohydrate is divided approximately in these meals on the basis of 2/7, 2/7, 2/7 and 1/7.

Breakfast	Lunch	Dinner
Grapefruit—½	Toasted cheese sandwich	Roast leg of lamb—4 oz. (113 Gm.)
Soft cooked egg—1	American cheese—1 oz. (28 Gm.)	Carrots—½ cup
Oatmeal—½ cup	Bread—2 slices	Mixed green salad
Whole wheat toast—1 slice	Fat—1 tsp.	Small potato—1
Butter or oleomargarine—1 tsp.	Tomato salad	Bread, white, enriched—1 slice
Milk—1 cup	Prunes—2	Butter or oleo—1 tsp.
Coffee	Tea	Orange slices
		Coffee

Night Lunch

Milk—1 cup and graham crackers—2

Table 2 summarizes the carbohydrate, protein and fat content of the various food equivalents listed in table 1. By the use of this table it is possible to calculate diet prescriptions with considerable ease and simplicity, taking into account the amounts of each of these food groups which the patient is desirous of eating. Nutritive adequacy of the diet is generally assured by seeing that at least one or more items from each of these food groups is included in the diet and by selecting a variety of vegetables and fruits in order to supply daily a serving of a green or yellow vegetable and of a fruit or vegetable which is a good source of ascorbic acid. Variety in the diet is achieved by making use of the food equivalents.

Tables 4 and 5 are specific examples of the use of this method in calculating a diet for a patient with diabetes.

To determine the number of servings of carbohydrate equivalents or fat equivalents required to complete the diet prescription, it is necessary only to:

1. Subtract the number of grams of carbohydrate (68) furnished by the other sources of carbohydrate in the diet from the amounts prescribed (180) and divide the result by 16, the number of grams of carbohydrate in one serving of carbohydrate equivalent.

2. Follow the same procedure with regard to fat, except to divide the result by 4, the number of grams of fat in one serving.

The amount of protein in any diet may be adjusted to the prescription by adding or subtracting 1 ounce (28 Gm.) of meat or its equivalent.

Table 6 gives a sample day's menu which is based on the foregoing diet outline and makes use of the food equivalents in table 1.

CONCLUSION

A simplified method for the rapid calculation of diabetic diets has been presented which should be of help to the busy practitioner.

INHERITANCE OF RETINOBLASTOMA

Two Families Supplying Evidence

HAROLD F. FALLS, M.D.
Ann Arbor, Mich.

It is my purpose in this paper to present two new pedigrees which lend support to evidence that retinoblastoma is a hereditary form of neoplasia. An increased interest in the genetic determination of such tumors has been evidenced in the medical literature of recent years. Weller [1] in 1941, Griffith and Sorsby [2] in 1944 and Rados [3] in 1946 carefully reviewed and analyzed the evidence that such malignant neoplasms of childhood may be the results of hereditary factors.

Weller cautiously concluded that there is no clearcut evidence to demonstrate that the predisposition to retinoblastoma behaves either as a simple dominant or as a simple recessive trait. This author postulates an inheritance of a somatic variation, possibly a structural anomaly, on which retinoblastoma may or may not develop. It was further suggested that retinoblastoma may belong to those congenital new growths which have been termed the "phakomatoses."

Griffith and Sorsby concluded that the tumor may be due to an irregular dominant gene; that is, to one which produces the neoplasm in a certain proportion but not in all of the heterozygotes who receive this gene. Waardenburg [4] states that in addition to domi-

An investigation supported in part by research grants from the Horace H. Rackham School of Graduate Studies, University of Michigan.
Read before the Section on Ophthalmology at the Ninety-Fifth Annual Session of the American Medical Association, San Francisco, July 4, 1946.

1. Weller, C. V.: The Inheritance of Retinoblastoma and Its Relationship to Practical Eugenics, Cancer Research **1**: 517, 1941.
2. Griffith, A. D., and Sorsby, A.: The Genetics of Retinoblastoma, Brit. J. Ophth. **28**: 279, 1944.
3. Rados, A.: Occurrence of Glioma of Retina and Brain in Collateral Lines in Same Family, Arch. Ophth. **35**: 1 (Jan.) 1946.
4. Waardenburg, P. J.: Das menschliche Auge und seine Erbanlagen, The Hague, M. Nijhoff, 1932.

nant inheritance a recessive gene may account for certain cases wherein consanguinity has been demonstrated in normal parents.

Observations on twins, and particularly on monozygotic twins, are of special value in human genetic research. These studies aid in assessing the role of heredity in the production of the trait being studied. Since identical twins are derived from a single fertilized ovum, they must have precisely the same genetic constitution or genotype. When monozygotic twins have similar tumors in identical organs at approximately the same age, much credence must be given to the role played by heredity in the determination of that tumor. It is of interest that the literature contains two carefully studied monozygotic twin pairs [5] in which both members exhibit retinoblastoma.

The two families which I shall describe have not previously been reported. They constitute Kindreds 502 and 574 in the files of the University of Michigan Heredity Clinic.

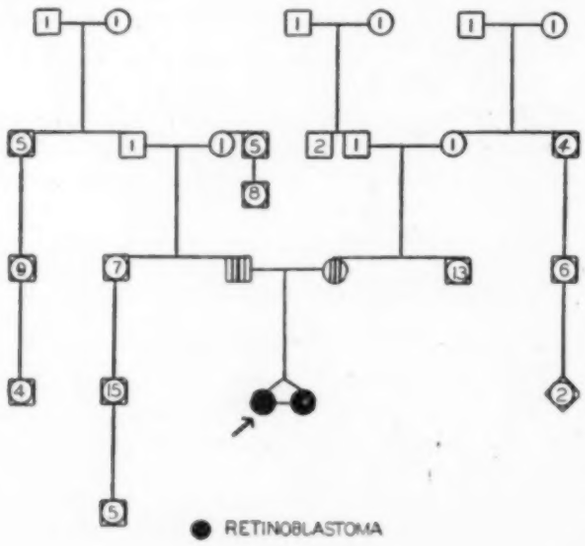


Fig. 1.—Kindred 502.

KINDRED 502

The pedigree chart reproduced in figure 1 follows the conventional plan of arranging siblings on a horizontal line in the order of their birth. All examined individuals were subjected to careful ophthalmologic study, and, in addition, data were secured on the color vision, A-B-O blood types, M-N blood types, secretor types and taste reaction to phenylthiourea.

The propositae for pedigree 502 are thought to be identical twins because they possessed a "single cord" and an identical blood type (OMN) and were remarkably similar in body proportions, facial features and pigmentation. Since the mother belonged to blood group OM and the father to group BMN, it will be seen that the twins could have been of different A-B and M-N types as well as of different sex had they been derived from two separate fertilizations.

The parents were of French and of Scotch-English descent. There was no known family history of ocular neoplasia, and evidence of consanguinity could not be obtained. Examination of the grandparents and aunts and uncles was refused because of certain prejudices.

5. Benedict, W. L.: Retinoblastoma in Homologous Eyes of Identical Twins, Arch. Ophth. **2**: 545 (Nov.) 1929. Duncan, W. J. L., and Maynard, R. B. M.: Bilateral Glioma in Twins, Tr. Ophth. Soc. Australia **1**: 125, 1939.

CLINICAL PATHOLOGY

1. C. J. LaB., a girl aged 6 months, was first seen at the University Hospital Ophthalmic Clinic on July 26, 1943, at which time the parents had become alarmed about an apparent lack of vision which they had first noticed in the child at the age of 4 months. Physical examination showed that the length of body was 23¼ inches (59 cm.) and the weight 13 pounds (6 Kg.). The head was symmetrical. The anterior fontanel was patent and presented normal tension to palpation. The head circumference was 16 inches (41 cm.). The neck and thorax were normal and symmetrical. The heart rhythm and rate were normal. The lungs were clear. Neurologic abnormalities were not demonstrated.

The eyes showed eccentric wandering but would attempt light fixation. The external examination was normal bilaterally. Evidence of inflammatory change was not found. The lens and central media of the right eye were clear. The disk was oval vertically and of fair color and capillarity. Encroaching on the temporal disk margin and extending laterally across and beyond the macular area for at least 8 to 9 disk diameters was an extensive gelatinous pinkish gray mass. Many newly formed vessels were observed in the growth, which extended into the vitreous for nearly 10 diopters. The remainder of the retina and its vasculature seemed normal. The intraocular tension was normal to palpation. Examination of the left eye revealed conditions similar to those of the right eye except that an additional smaller mass was seen just above and slightly nasal to the disk.

The diagnosis was bilateral retinoblastoma.

Roentgenologic examination of the orbits revealed minimal intraocular calcification in both eyes.

Enucleation of the right eye was advised for the purpose of pathologic study. The parents refused and wished to consider the alternative suggestion of roentgenotherapy before permitting hospitalization. During the course of the conversation it was revealed that C. J. had a twin sister, K. J., and the parents were strongly urged to bring her to the clinic for examination.

2. K. J. LaB. was first seen in the private office of Dr. F. B. Fralick at the age of 11 months. The parents reported that a bilateral gray reflex had been observed at the age of 6 months but that they had procrastinated in returning for examination. The child appeared to be in a good state of health and nutrition, and the physical examination revealed no clinical pathologic changes.

Ophthalmologic examination revealed eccentric roving of the eyes. The external findings were normal except for unduly dilated pupils which reacted poorly to direct light. There was no evidence of inflammation of the anterior segment of either eye. The intraocular tension was normal bilaterally to palpation. Funduscopy revealed that the entire posterior segment of each eye was occupied by a pinkish gray gelatinous appearing mass which was abundantly vascularized.

The diagnosis was bilateral retinoblastoma.

Bilateral enucleation or roentgenotherapy was advised.

C. J. was also seen by Dr. Fralick at the same visit. It was reported that the child had shown symptoms of severe pain until spontaneous rupture had occurred at the age of 9 months. The globe collapsed, and soon the child grew more and more cachectic and constantly refused all feeding.

Ophthalmologic examination of the right eye disclosed that the anterior ocular segment was normal and that the posterior segment was filled with a tumor mass. Examination of the left eye revealed phthisis bulbi.

The parents refused therapy for C. J. and she died on March 5, 1944. Intracranial and posterior orbital extension was reported by a local physician.

Pathologic tissue obtained post mortem from the left eye was described by Dr. C. V. Weller as a collapsed eye showing productive inflammation and heavy calcification. The latter process was developing in the remains of a retinoblastoma, the greater part of which was necrotic. There was no evidence of penetration of the globe at the two sites examined.

K. J.'s course was much less spectacular than C. J.'s. The child gradually wasted away in cachexia until death ensued in June 1944. As in C. J.'s case, there was intracranial and

posterior orbital extension of the tumor, and pathologic tissue study of the left eye revealed retinoblastoma with extensive necrosis and calcification.

KINDRED 574

Interest in the second family was stimulated by Dr. Gayle Mehney of Grand Rapids, Mich., who courteously referred the proposita to the Heredity Clinic. Dr. Mehney had diagnosed retinoblastoma in the left eye of this girl at the age of 3½ years. Enucleation was performed by Dr. Alfred Dean, Grand Rapids, and pathologic examination confirmed the clinical diagnosis of retinoblastoma.

When a pedigree of the family (fig. 2) was secured, it was revealed that ocular tumors were common in the sibship of the child's mother. More interesting still was the fact that the mother had her left eye enucleated at the age of 3½ years because of retinoblastoma. Five of the 9 siblings had had a diagnosis of retinoblastoma. Two of those affected survived to reach child bearing age.

III-1.—O. K. T., a boy, was born Dec. 17, 1887 and died Nov. 23, 1890. At the age of 4 months the child's nurse observed a "peculiar reflex from the left eye." Many local physicians were consulted, but no one recognized the nature of the ocular growth. Severe and increasing proptosis ensued. At the time of death large growths were noted in the neck. Abnormality of the right eye was not observed.

III-3.—H. W. T., a boy, was born on May 27, 1891 and died on July 21, 1891. It is reported that this child's left eye was involved in a manner similar to that of his brother, III-1. An enucleation was adivsed, but the parents procrastinated and death quickly followed. The globe was decidedly proptosed at death. The type and nature of extension were not recalled or recorded. It is thought that the right eye also was involved.

III-5.—A. R. T., a woman aged 52, born Sept. 1, 1894, reported an abnormal "light" was noted in the pupil of her left eye at the age of 2½ years. A diagnosis of retinoblastoma (glioma) was made by a local physician, and the eye was enucleated at 3½ years of age. The pathologic diagnosis was given as "glioma of the retina." This woman's only child, a daughter, aged 26, was found to be free of ocular tumors.

III-8.—J. M. T., a boy, who was born June 8, 1904 and died March 6, 1907, was known to have a defective left eye at the age of 1½ years. The eye was enucleated at 2 years of age, and "glioma of the retina" was the pathologic diagnosis. The vision in the right eye was reported as defective, but a description of the pathologic condition of the retina is not available. The presence of abdominal swelling at death suggests possible metastasis to the liver.

III-0.—A. M. T., a woman born Dec. 21, 1907, is the mother of the propositus. The tumor in her left eye was observed by a local physician when she was 3½ years of age and pathologic study of the enucleated eye revealed "glioma of the retina." Our physical and ocular examination in 1944 did not reveal any pathologic condition other than ocular prosthesis in the left orbit.

It is thought that II-1 died of a carcinoma of the stomach, and it is known that I-1 had a large pigmented nevus of the neck and arm. Death of the latter person was attributed to "apoplexy."

COMMENT

Pedigree 502 presents evidence of bilateral retinoblastoma in female identical twins occurring at approximately 6 months of age in both. In the absence of surgery or roentgenotherapy, a fairly rapid intracranial extension of the tumor led to the death of both children. This is the third reported instance wherein retinoblastoma has occurred in both identical twins.

Pedigree 574 contributes another family to the growing list of reported observations of the "vertical transmission" of the neoplasm.

One cannot be dogmatic in stating the mechanism of inheritance of retinoblastoma. In many of the reported pedigrees it appears that the tumor may be transmitted as an irregular dominant trait affecting only a portion of the gene carriers. Other families, however, could be interpreted as exhibiting a simple recessive mendelian pattern. That various types of inheritance may be encountered for a specific disease, in this instance retinoblastoma, is not unusual, for it is rather common to find that the same phenotype may have different genotypes. Macular degeneration of the retina, various forms of cataract, corneal dystrophy, glaucoma and retinitis pigmentosa are only a few of the human ocular anomalies which exhibit this phenomenon.

Since retinoblastoma is so frequently lethal at an early age, natural selection should be operating rather effectively against genes producing this tumor, provided the parents of such children do not make up this loss by increasing their fertility. If it is further assumed that the tumor is not rapidly on the decline, its incidence in the population is probably being sustained by a certain number of mutations or "new genes" in each generation. One should therefore expect a certain number of sporadic cases of retinoblastoma arising by

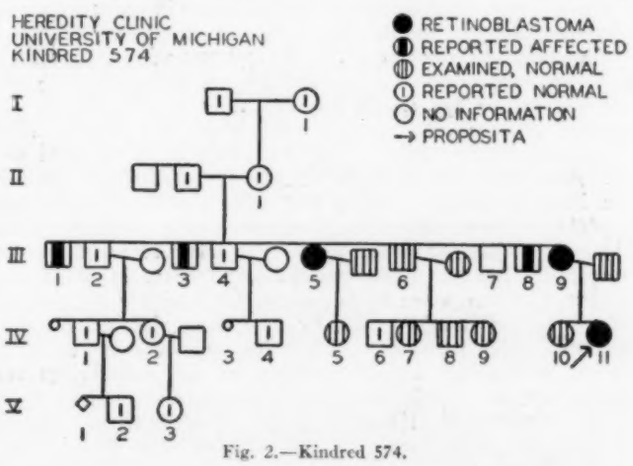


Fig. 2.—Kindred 574.

mutation, and the case of twins described in this report may represent such an instance. A mutation, occurring either in oogenesis or in spermatogenesis, would account for both twins being affected.

It is my sincere conviction that parents producing any child with retinoblastoma should be strongly urged to stop all child bearing. It is also advocated that any person surviving enucleation for retinoblastoma be sterilized.

The pathologic material encountered in both families was handled largely by outside sources, and in the case of pedigree 573 the material is no longer available. This is unfortunate, since it would have been of interest to compare the histologic appearance of the obviously inherited type of retinoblastoma with that of the occasional "sporadic" tumor. Cummings and Sorsby[6] could not discover any difference between the histologic character of a sporadic bilateral retinoblastoma and that of a proved genetic bilateral neoplasm.

SUMMARY

1. A family was observed in which retinoblastoma occurred bilaterally in identical female twins.

2. In a second family both the horizontal and the vertical occurrence of retinoblastoma was observed.

6. Cummings, J. N., and Sorsby, A.: Unilateral and Bilateral Retinoblastoma, Brit. J. Ophth. **28**: 533, 1944.

3. Retinoblastoma may have different genotypes, and it is not necessary to interpret all pedigrees in terms of a single mechanism of inheritance.

4. Parents who have produced a child with retinoblastoma should be urged to discontinue having children, and children surviving enucleation for retinoblastoma should be sterilized.

ABSTRACT OF DISCUSSION

DR. A. B. REESE, New York: I should like to cite two tragic instances illustrating the practical importance of what Dr. Falls has said. A father who in infancy had had both eyes enucleated because of retinoblastoma was not told of the danger of reproducing the disease, and his only child had bilateral retinoblastoma and bilateral enucleation. The child survives now after several years. A father who had bilateral retinoblastoma and bilateral enucleation in infancy was advised after marriage that it would be safe to have children. The first child had bilateral retinoblastoma and bilateral enucleation and now survives. Before the fate of the first child was known, a second child was conceived. This child also has bilateral retinoblastoma, for which an enucleation has been done on the more advanced eye. The fellow eye is being irradiated.

DR. C. WILBUR RUCKER, Rochester, Minn.: Dr. Falls, in presenting these two new pedigrees, has made a further important contribution to the literature on the inheritance of retinoblastoma. He points out that the tumor may be inherited in any one of a variety of ways in different families and that in some instances it seems to appear as a spontaneous mutation. Painstaking studies, such as this, should lead to a clearer conception of the various modes of inheritance of this disorder and should enable physicians of the future to give more helpful advice than we can give now. In the light of present knowledge certainly Dr. Falls is correct in urging that parents who have produced a child with retinoblastoma discontinue having children and that persons who survive enucleation for retinoblastoma remain childless. Toward the latter group, however, he is taking a hazardous step when he advocates sterilization during childhood. Society would benefit by it without a doubt, but the physician who performs a sterilizing operation on a child, in the absence of a specific statute to the contrary, makes himself liable to suit for assault, instituted by the patient when he reaches the age of 21 years. It would be my opinion that the physician should not risk the possibility of a ruinous legal suit, even for his convictions about eugenics, and that he had better content himself with giving advice on the use of contraceptives.

DR. HAROLD F. FALLS, Ann Arbor, Mich.: Retinoblastoma-like lesions have been produced by synthetic substances. In this respect it is important to state that the genes are complex chemicals and thus effect mutant changes, possibly in a manner similar to that of noxious agents. It is impossible for the clinician to differentiate, in many isolated cases, whether the anomaly in question is the effect of a genetic influence or that of a noxious chemical or physical factor. Dr. Rucker has suggested that it is legally dangerous to advise sterilization of minors. I agree, but, for the benefit of the race and also for the respective families to prevent the misery, the pain and the discomfort to both the parents and the affected individual, I would strongly emphasize the advocation of sterilization. We as physicians can only advise; the initiative falls on the parents.

Bacterial Endocarditis.—The success of the treatment of subacute bacterial endocarditis lies first in early diagnosis, which is hastened and confirmed by obtaining blood cultures three times daily for three successive days; second, in prolonged treatment with penicillin in adequate dosage; third, management of the cardiac failure; fourth, employment of general measures, especially blood transfusions and replacement of serum proteins; and, fifth, in the use of in vitro studies, which are of inestimable value in prognosis and in governing the course of therapy.—McMillan, Robert L.: Subacute Bacterial (Streptococcus Viridans) Endocarditis Treated with Penicillin, *Am. J. Med.*, December 1946.

Special Article

HISTORY OF THE AMERICAN MEDICAL ASSOCIATION

MORRIS FISHBEIN, M.D.
Editor, Journal of the American Medical Association and Hygeia, the Health Magazine
Chicago

(Continued from page 104)

(NOTE.—*Following is the eleventh chapter of a history of the American Medical Association, in process of development for publication in connection with the celebration of the Centennial of the American Medical Association in Atlantic City in June 1947.*

The general account of the history of the Association will be followed by individual histories of the various councils, bureaus, publications and other activities of the Association. The general account is written by the editor of THE JOURNAL. *Each of the other historical contributions will be by a member of the individual council, bureau or agency responsible and now associated with it or directly related to its work. Included will be photographs, signatures and a brief biography of each of the hundred presidents of the American Medical Association. This feature has been prepared by Dr. Walter L. Bierring.*

It will be impossible to publish all of the material in THE JOURNAL. *The complete work will be published in book form. It is hoped to have it available by the time of the annual session.*—ED.)

CHAPTER 11. *Growing Pains, 1875 to 1879*

1875

LOUISVILLE, KY.

The special committee on rank of the medical corps of the Army reported that it had used extraordinary efforts but had been unable to secure any action whatever from Congress. The Surgeon General of the Army expressed his thanks and his regret that nothing had been done; he was sanguine that in the long run the Army Medical Department would be successful if the American Medical Association would continue to take the same interest in the future as it had in the past.

Dr. J. Marion Sims was elected to the presidency of the Association.

Most important of the resolutions adopted was the determination that each year, until otherwise ordered, the President-Elect and permanent Secretary should direct an appeal in the name of the Association to the authorities of each state without a board of health, urging them to establish such boards. The Secretary was to report annually the names of states in which boards of health existed and also those which declined to establish them.

As a supplement to the annual Transactions the prize essay on "Excision of the Larger Joints of the Extremities" by H. Culbertson, M.D., was made available to the members.

1876

PHILADELPHIA

The celebration of the centennial of the United States was notably observed by the meeting in Philadelphia in 1876. The delegates were welcomed by Dr. William Pepper. He called attention to the tremendous progress that had been made by Philadelphia, which now boasted of 820,000 inhabitants and had the lowest rate of mortality of any city in the world with over half a million inhabitants. He felt that this was largely due to the

lack of overcrowding in the city. Especially recommended to the delegates was a visit to the International Exposition then going on in Fairmount Park.

The President's address had dealt in part with syphilis; a motion was passed that 10,000 copies of that portion of his address be reprinted and distributed widely among the membership of the Association.

DR. SARAH HACKETT STEVENSON

At the meeting in Philadelphia in 1876, Dr. Sarah Hackett Stevenson was a delegate from the state of Illinois. She was the first woman member of the American Medical Association. When her name was called in the roll call, Dr. William Brodie of Michigan moved that the names of all female delegates be referred to the Judicial Council. This was on motion laid on the table. Dr. Stevenson, perhaps with remarkable wisdom, must have sat peculiarly quiet throughout the session since her name does not appear as a participant in the making of motions, the offering of resolutions the discussion of any papers or the presentation of any contribution.

Sarah Hackett Stevenson was born at Buffalo Grove, Ill., Feb. 2, 1849. She graduated from the Women's Medical College of Northwestern University and in 1874 went to Europe for two years' study where she worked with Huxley and Darwin. She began to practice in Chicago in 1876 and was sent as a delegate to the annual meeting of the American Medical Association in Philadelphia during that year. She was also the first woman to serve on the staff of the Cook County Hospital.

CONDEMNATION OF CULTISM

Another resolution suggested that members of the medical profession who in any way aid or abet graduation of medical students in irregular or exclusive systems of medicine are deemed thereby to violate the spirit of ethics of the American Medical Association.

STATE BOARDS OF HEALTH

The Secretary reported that boards of health "now exist in Alabama, California, Massachusetts, Michigan, Minnesota, Virginia and Wisconsin—but eight states in all." A careful counting will reveal only seven states listed as having state boards of health. He stated further that the matter was still being urged on the legislatures of the other states.

THE PHARMACOPEIA

Significant also was a resolution introduced by Dr. E. R. Squibb urging the American Medical Association to take the whole subject of the National Pharmacopeia into consideration for a review of its management. Dr. Squibb was requested to reduce to writing his plan for the Pharmacopeia. He found that already an interval of ten years embraced so much detail that it was becoming impracticable to handle it. It was his feeling that perhaps the American Medical Association should be the proper custodian of the Pharmacopeia and that perhaps the American Medical Association should take the leadership and invite cooperation of the American Pharmaceutical Association.

ADDRESS BY DR. J. MARION SIMS

In his presidential address Dr. J. Marion Sims recalled the meeting in Philadelphia in 1872 when so much time was wasted in discussing the woman physician question and the Negro question. He asserted that the Association was a truly representative body and that if any state or county medical society should send as a delegate either a woman or a Negro, the Association was bound to receive the delegate. He felt that the creation of the Judicial Council was a great step in advance in overcoming local problems of ethics which were a great source of annoyance and danger. Dr. Sims condemned particularly the system of education in which first, second and third year students sat side by side on benches at the same time and heard the same lectures year after year. He said:

> Already Chicago moves in the right direction; but Boston now takes the lead, and inaugurates the true scholastic method of classes, and terms of study, and courses of practical instruction, now fully appreciated by such young men as are in earnest in acquiring a thorough medical training.
>
> The Harvard method, with a salaried Faculty wholly independent of fees from students, is the only plan by which we can ever hope for a medical degree of any real value.

He urged the wealthy men of the country to increase the endowments of the medical schools. In his consideration of the Code of Ethics he doubted its significance, its validity or its constitutionality. It was susceptible of being used as an agent of persecution. "Let it stand as it is," he said. "Honorable men do not need its protection; dishonest men are not influenced by its edicts."

He urged widespread publicity concerning syphilis, which he considered the great problem of the day.

J. Marion Sims was opposed to licensure of prostitution as effective in the control of venereal disease. His answer was a system of sanitary inspection and control that would enable the health officer to take charge of those with syphilis and prevent them from spreading it through the community. Boards of health ought to have power to protect the public against all contagious and infectious diseases. He said he would simply include syphilis in the great family of contagious or communicable diseases and make it subject to the same laws and regulations used for their management.

1877

CHICAGO

Dramatic indeed was the opening of the meeting of the American Medical Association in Chicago on June 5, 1877. Dr. N. S. Davis welcomed the delegates; the Transactions said "Thirty-one years ago seventy-six gentlemen met in New York, representing the medical profession in the United States. Two thirds of the members have passed away, and he now failed to recognize a single face, in the meeting today, that was present on that occasion." At that moment a hand was raised, and Dr. N. S. Davis recognized Dr. Washington L. Atlee of Philadelphia, the only physician present who was one of the original seventy-six. Only twenty-nine years had passed since the organizational meeting in New York City, and yet that twenty-nine years had seen the departure from life of many of the great leaders of the previous generation.

ADDRESS OF DR. HENRY I. BOWDITCH

The President of the Association, Dr. Henry I. Bowditch of Boston, pointed out that the American Medical Association had united the physicians of the country, ironed out local idiosyncrasies and brought together men from every section. He remembered that wine flowed freely at public and private gatherings of an earlier day and that there had been occasional disorder observable during the debates but that the Association from this disorder had cemented friendships, so that it became one of the bulwarks of the state and a help toward civilization on this continent. By 1876 he felt, however, that the American Medical Association

had lost repute in the Eastern and Middle states and with some of the leaders of the Western and Southern states. This, he felt, was due to two general causes: (1) the furious discussions on points of order and the ethics of professional etiquette and (2) the consciousness that the Association had been expected to produce results in the advancement of medicine and of professional stature out of all reason. He felt also that some of the meetings of the scientific sections had been used for the presentation of "papers or remarks from individuals, smitten with the *cacoethes scribendi aut loquendi*" and that they had not always had the ability or the will to check them. He also felt that the Transactions of the Association were too bulky and included now some papers that had been printed elsewhere and really constituted nothing in the way of advancement.

Another cause of disturbance was the passage of resolutions with lack of sufficient information, but which, nevertheless, compromised the entire Association. Finally, it was claimed, the Association was too democratic. Having ventured these criticisms, Dr. Bowditch offered suggestions for the improvement of the sections and for procuring scientific contributions. He praised highly the work of the Judicial Council in its settlement of questions of dispute. He urged that the social meetings include women and abandon alcoholic drinks.

He urged also, for the first time, that every member of a state medical society become a permanent member of the American Medical Association. Finally, he suggested a smaller delegation in the House of Delegates as representative of the membership.

The remainder of his address dealt with the possibility of association with the Canadian Medical Association and with the Pharmacopeia. He urged support for the Army Medical Library and Museum and of the American Medical College Association.

This address having been referred to a special committee, a report was received leading to improvement of the sections. The committee did not favor any change in the present plan of organization and considered association with the Canadian Medical Association impracticable.

The meeting in Chicago in 1877 was most impressive to Dr. Charles B. Johnson, who attended as a delegate from the Illinois State Medical Society at Champaign, Ill. The meeting was in the Palmer House and there were no elevators, so that guests climbed to the top stories. Dr. Johnson recalled seeing the venerable Dr. S. D. Gross of Philadelphia mounting the stairs laboriously. Dr. Gross stopped for a brief chat with Dr. J. Marion Sims, who had been President the year previously, and Dr. Johnson heard the renowned gynecologist say that "if he had his professional life to live over he would by hook or crook try to get more money out of it."

The address of Dr. Bowditch he remembered for a long time because of the recommendation that the American Medical Association conventions be conducted on temperance principles.

When Dr. Bowditch attended the meeting of the American Medical Association in Chicago in 1908, one of the sessions was held in a German hotel and the refreshments consisted of beer and pretzels. He tried to get a cup of coffee, but the waiter told him it could not be had. Then he asked for a glass of water. The waiter looked at him in astonishment but finally served the water.

PHARMACOPEIA VS. DISPENSATORY

At this point Dr. E. R. Squibb of New York presented a report on the revision of the Pharmacopeia. The underlying grievance was a personal matter between Dr. Squibb and Dr. H. C. Wood of the U. S. Dispensatory. Dr. Squibb began to read at 10 o'clock and was still reading at 11 o'clock. After another considerable period, a motion was made that Dr. Squibb be permitted to resume on Thursday at 12 noon and be given twenty minutes in which to finish his remarks. The remainder of the session was to be given to those entertaining opposite views to those of Dr. Squibb.

Intervening was a prolonged discussion on representation of homeopathic groups and the licensure of homeopathic physicians in various states.

When Dr. Squibb again began reading his address it was discovered that he could not conclude, and he was given additional time. He continued reading until the expiration of this additional time, and then, since he had not concluded, the Association proceeded to elect its officers.

Following the election by vote, a committee of five was appointed to examine the papers of Dr. Squibb and of Dr. Wood and of others and to determine the extent to which the American Medical Association should participate in the Pharmacopeia.

THE STATE BOARDS OF HEALTH

On the final day of the session, attention was called to the fact that the American Medical Association through its President and Secretary had urged the governor in every state to establish a state board of health. A resolution was passed urging the President and the Secretary of the Association to continue such an appeal year after year to the governor in every state until such state boards of health should be established. This was one of the most fundamental contributions made by the American Medical Association to the advancement of public health in the United States.

NEW SECTIONS

Now came appeals for the establishment of a new section on ophthalmology, otology and laryngology, since these specialties had assumed full stature with surgery and internal medicine.

INCREASED MILITARY MEDICAL RECOGNITION

A report was made from the committee that had urged on the Congress the establishment of better recognition of the medical staff of the U. S. Army. By this time the efforts of the committee had achieved some success. A letter from Surgeon General Joseph K. Barnes of the U. S. Army thanked the committee and expressed appreciation of the influence exerted in behalf of the medical officers of the Army by the American Medical Association.

1878

BUFFALO

Extensive reports were made by the delegates who had visited the Canadian Medical Association, the British Medical Association and the International Medical Congress of Geneva. The report from Geneva urged the possibility of developing a uniform pharmacopeia throughout the world—an ideal still sought in 1946 by the Health Organization of the United Nations.

HOMEOPATHIC PROBLEMS

The Judicial Council presented to this meeting charges against the Michigan State Medical Society for having elected as a delegate to the American Medical

Association one Dr. E. L. Dunster of the University of Michigan "knowing him to be engaged in aiding and abetting the graduation of students devoted to an exclusive dogma in medicine." Nothing had been found in the Principles of Ethics which would bear directly on the charges. From time to time resolutions had been adopted referring to the practice of cultism, but these resolutions did not constitute a part of the Code of Ethics. This report was discussed freely. Finally, a motion was made asking the Judicial Council to report at a subsequent meeting a law to meet the case in question.

At the meeting of the next day, Dr. Nathan Smith Davis proposed the following addition to the Principles of Ethics:

> And hence it is considered derogatory to the interests of the public and the honor of the profession, for any physician or teacher to aid, in any way, the medical teaching or graduation of persons knowing them to be supporters and intended practitioners of some irregular and exclusive system of medicine.

ORGANIZATIONAL PROGRESS

The Buffalo meeting elected Dr. Theophilus Parvin, then of Indiana, President.

An extensive report by a committee of N. S. Davis and S. D. Gross concerned the recommendations made by the President, Henry Bowditch, in the year previously. These two leaders were not inclined to accept the suggestions of Dr. Bowditch as to changing the nature of membership in the House of Delegates. They had some alternative proposals as to the selection of papers for the sections and as to the decisions on publication of papers. Dr. Bowditch submitted for himself a minority report disagreeing with them, but the majority report was adopted.

Ultimately the ideas of Dr. Bowditch as to representation in the House of Delegates and the consideration of papers read in the sections prevailed. The improvement in general quality of the medical profession, the raising of medical standards, the organization of the state medical societies and the advancement of medical science made the suggestions wholly logical.

The committee which had been urging the establishment of state boards of health was happy to announce that three additional states had founded boards of health so that now there were nineteen in all.

RESTRAINT OF THE INSANE

Psychiatry was discussed, and a resolution was adopted that the personal restraint of the insane is an essential element in the treatment of their disease. Nevertheless it was recognized that the state had a right to surveillance or legal regulation over restraints on the insane in order to punish any abuses of the right of restraint.

The report on the Michigan State Medical Society and Dr. Dunster indicated that there was no law by which the Michigan State Medical Society could be found in conflict with medical ethics. Immediately thereafter an amendment to the Principles of Ethics was adopted as previously suggested, and this took care of the situation.

PROMOTION OF THE PUBLIC HEALTH

In his presidential address Dr. T. G. Richardson paid attention to the improvement in the sections. The most significant portion of his address dealt with the creation of the state boards of health and the prevention of illness as their proper field of activity. He urged particularly better education of the public in regard to health and spoke with scorn of the gentleman who took his 14 year old daughter out of a first class school because a human skeleton was brought into the classroom by the professor of physiology, who was going to teach the pupils a few facts in regard to respiration and circulation. Dr. Richardson opposed federal control of public hygiene, but he recognized the necessity for a federal agency to prevent the introduction of contagious and infectious diseases from abroad. The 45th Congress had taken the first action since 1799 toward enforcing public health laws. Here is the concluding paragraph from Dr. Richardson's address:

> Whatever doubts there may be as to the extent of the authority possessed by the central government, there seems to be no dispute that within the limits of each separate state resides a power which with reference to all such matters is practically supreme. It is to this power represented by the legislature and executive of each state that we must look for the enactment and enforcement of such laws as state medicine demands of a wise government, economical not less of the lives and health of its citizens than of its material resources. It is therefore upon this power that the state medical societies should concentrate all their influence, professional and social, to effect the necessary legislation. They should employ their best endeavors to have state boards of health created where these do not exist, and they should by all means secure the right of nomination for appointment upon such boards; otherwise positions which demand men of peculiar qualifications and sterling integrity will be conferred, as is too often the case, upon mere office hunters, who have no interest whatever in the matter beyond its pecuniary return.

1879

ATLANTA, GA.

Organizations fall into strange traditions of action; patterns are followed until suddenly comes realization of hazard on the path. Dr. Joseph P. Logan of Georgia, who welcomed the delegates to Atlanta on May 6, 1879, stated frankly that he had looked up the previous copies of the Transactions of the American Medical Association to discover how an address of welcome ought to be made. He decided to do a job for Atlanta which "has sprung, in little more than a decade, into a city of 40,000 people." Remember that Atlanta had been devastated by the war. "We have not, however, my friends, sat down in ignoble lamentations over our misfortunes, but have gone to work with energy and determination to rebuild and make better our desolated places." These words are the beginning of a sentence which then continues without interruption for sixteen printed lines having to do with the industries, the works and the climate of Atlanta.

THE METRIC SYSTEM

The report on the International Medical Congress pointed out that the United States Marine Hospital services had adopted the metric system, which was found to work very well, and that it had been adopted by all nations except two—the United States and England. Later in the session a resolution was adopted that the metric system be official and be used in the Transactions. The agitation regarding the metric system was to go on and on for many years; the end is not yet.

A message of congratulation was sent from the convention to Ohio which had passed a bill making possible the dissection of human bodies.

The Association was still disturbing itself as to how to get some prize essays written that would be worthy

the name; now four prizes of $250 each were established for strictly original contributions to medical and surgical progress.

ETHICAL RELATIONS AND CULTISM

Especially significant was the debate on the amendment to the Principles of Ethics having to do with exclusive systems of medicine. Because the attendance in Atlanta was small, the resolution was permitted to lie over until the following year.

The representative body also heard of action taken by the section on state medicine and public hygiene in response to an address by Dr. John Shaw Billings on securing statistical data on disease and mortality.

NOTE ON PROPRIETARY MEDICINES

A resolution was offered and referred to the Judicial Council protesting the placing on the market of drugs and combinations of drugs with copyrighted names. This seems to be the first mention of the practice which bore bitter fruit for the American people for many years.

The presidential address of Dr. Theophilus Parvin declared that medicine was the queen of the sciences. He then discussed the philosophy of science and of medicine with sixty references to bibliographic material. It seems to constitute the most learned document presented up to that time as a presidential address; but it concerned itself not at all with any immediate affairs. One reads it again and again puzzling over its meaning and significance, and at last one thinks of that stanza of Omar Khayyam:

> Myself when young did eagerly frequent
> Doctor and Saint, and heard great argument
> About it and about: but evermore
> Came out by the same door wherein I went.

(To be continued)

Clinical Notes, Suggestions and New Instruments

AVOIDANCE OF ALLERGY TO LIVER EXTRACT

C. J. SULLIVAN, M.D., and G. O. BROUN, M.D.
St. Louis

One of the difficulties encountered in the treatment of macrocytic anemias with liver extract has been the development in occasional patients of allergic reactions to the liver extracts employed. Schwartz and Legere [1] in a recent article suggested that such allergic reactions may be avoided by changing the "brand" or type of liver extract, by reducing the dose of liver extract, by desensitizing with liver extract or by utilizing a histamine-protein complex as an antigen to produce histamine antibodies. The successful use of folic acid in the treatment of macrocytic anemias [2] suggests the possible value of this material in avoiding the effects of allergy to liver extract.

We have recently observed a patient suffering from addisonian pernicious anemia whose course was complicated by the presence of allergy to liver extract administered by parenteral injection. The sensitivity appeared to be organ-specific rather than species-specific since both hog liver and beef liver produced anaphylactic-like reactions. A minute dose of hog liver produced an immediate mild allergic reaction. A change to beef liver was effective in the avoidance of an allergic reaction as long as the dose was kept small. A large dose produced a severe allergic reaction. Folic acid therapy was instituted with dramatic and satisfactory response. In order to obtain maximum erythrocyte and hemoglobin levels, dosages of dried stomach extract and iron and sodium citrate were added to that of folic acid. The patient has been rendered free of symptoms and maintained at an erythrocyte level of more than 4,000,000 per cubic millimeter, with more than 13 Gm. of hemoglobin per hundred cubic centimeters of blood. The period of observation extended over eighty days of folic acid therapy.

From the Department of Internal Medicine, St. Louis University School of Medicine, and the Medical Service of the St. Mary's Group of Hospitals.

1. Schwartz, S. O., and Legere, H.: Treatment of Liver Extract Sensitivity, Blood **1**: 307, 1946.

2. Spies, T. D.; Vilter, C. F.; Koch, M. B., and Caldwell, M. H.: Observations of the Anti-Anemic Properties of Synthetic Folic Acid, South. M. J. **38**: 707, 1945. Moore, C. V.; Bierbaum, O.; Welch, A. D., and Wright, L. D.: The Activity of Synthetic Lactobacillus Casei Factor ("Folic Acid") as an Anti-Pernicious Anemia Substance, J. Lab. & Clin. Med. **30**: 1056, 1945. Doan, C. A.; Wilson, H. E., Jr., and Wright, C. S.: Folic Acid (L. Casei Factor) an Essential Pan-Hematopoietic Factor: Experimental and Clinical Studies, Ohio State M. J. **42**: 139, 1946.

REPORT OF CASE

History.—Mrs. C. C. was admitted to the University Hospital on March 30, 1946 complaining of weakness and pain in the legs. For the past four years she had been receiving from her physician injections of liver extract at regular intervals for treatment of anemia. In November 1945 within fifteen minutes after she had been given an injection of liver extract, itching of the palms, edema of the face and tongue and dyspnea developed, and the patient soon became unconscious. Epinephrine was administered and she recovered, gradually returning to normal during the subsequent forty-eight hours. Parenteral injections of liver extract were then discontinued, and liver extract and ferrous iron were given by mouth. During the next four months her anemia became progressively worse, and she noted profound weakness.

For many years she had had varicosities of both legs. In September 1943 a localized, tender mass had developed in the left femoral region, which had been treated by rest in bed and by the application of ice bags to the affected part. During the month preceding this hospital admission she had been experiencing, at irregular intervals, sensations of substernal constriction of gradual onset, associated with faintness and profound weakness. There was, in addition, a sensation described as "bubbles" moving upward along the course of the veins of the legs, most noticeable at night in bed. Ten years ago she had undergone a hemorrhoidectomy. She had migraine for several years during early adult life and chronic constipation. Her past history was otherwise not relevant.

Physical Examination.—The patient appeared well nourished. The skin was a light lemon color; the hair was white. The general appearance was that of weakness and apathy. The tongue was pale and smooth, and the papillae were atrophic. The lips and oral mucosa were pale. There was sclerosis of moderate degree of the peripheral arteries. The blood pressure was 120 systolic and 60 diastolic. There was a soft systolic murmur at the cardiac apex. Dilated, tortuous, superficial veins were seen over the posterior, lateral and medial surfaces of both lower extremities, with one area of tenderness and increased heat over the medial aspect of the lower part of the left leg. The deep veins were found to be patent. Roentgenologic examination revealed that the heart was 17 per cent larger than the average normal with uniform widening of the aorta. Gastric achlorhydria was found. A proctoscopic examination did not reveal any abnormalities. Roentgenologic examination of the gastrointestinal tract showed slight herniation of the stomach through the esophageal orifice, a diverticulum of the jejunum and ptosis of the colon. Serial electrocardiograms showed only axis deviation to the left. Roentgenograms of the legs showed a slight degree of arteriosclerosis.

Hospital Course.—Since at the time of admission it was believed that the patient might be experiencing small pulmonary emboli, it was deemed advisable, in view of the physical observations and the past history of thrombophlebitis, to consider ligation of the veins of the legs. Dr. John W. Stewart saw the patient as a surgical consultant and recommended bilateral saphenous ligation. Accordingly, on April 1, 1946, two days after admission, the long saphenous veins on both sides were ligated at their junction with the femoral veins. The patient experienced postoperative shock, controlled by the administration of 1,000 cc. of whole blood. The accompanying chart

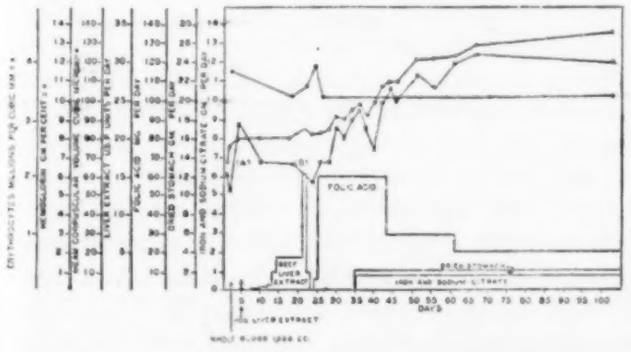
presents the antianemic medicaments used and the concomitant data on examination of the peripheral blood. It will be noted that liver extracts were at first administered in extremely small dosage, prepared by dilution of the original extracts.

COMMENT

This patient's type of anemia was macrocytic. The mean corpuscular volume determinations fell within a range between 118 and 102 cubic microns. The mean corpuscular hemoglobin concentration fell within a range between 32 per cent and 38 per cent. The presence of achlorhydria together with the absence of gross organic disease of the gastrointestinal tract or liver, and the history of an adequate dietary intake, justify by exclusion of other factors the diagnosis of addisonian pernicious anemia. It is of interest that the mean corpuscular volume and the mean corpuscular hemoglobin concentration have both remained at high levels at the termination of this period of observation, in spite of the absence of anemia.

Whole blood in the amount of 1,000 cc. was administered to combat postoperative shock. It will be seen from an inspection of the accompanying chart that this was followed by a sharp rise in the erythrocyte level, followed by a gradual decline. Three weeks later the erythrocyte count had declined to the pretransfusion level.

An extract of hog liver was administered in a single small dose (0.15 U. S. P. units). This was sufficient, however, to produce itching of the palms. It was probably a type of hog liver extract whose administration to the patient over a period



Response to various forms of treatment; *A*, allergic reaction, mild: itching of palms. *B*, allergic reaction, severe: itching of palms, vomiting, weakness and cold extremities, with persistence of symptoms for twenty-four hours.

of four years had eventually resulted in sensitization and shock, since most commercial liver extracts are hog liver preparations.

Beef liver extract was administered over a period of fourteen days. This extract was well tolerated by the patient as long as the dosage was small; in fact, a dose of 2 U. S. P. units given twice a day did not produce allergic reaction, whereas 0.15 U. S. P. unit of hog liver had done so. However, when 15 U. S. P. units of beef liver was administered a violent shock-like reaction occurred. It is of interest that the erythrocyte count fell progressively during the fourteen days of beef liver therapy. A transfusion of 1,000 cc. of whole blood had been given one week before the administration of beef liver was started. A distinct rise in the red blood cell count and hemoglobin level was noted five days after folic acid therapy was begun and before dried stomach was added to the therapeutic regimen. The erythrocyte count had increased by more than 1,000,000 cells.

The exact role played by the dried stomach can not be properly evaluated. This preparation was administered, together with iron and sodium citrate, after the initial rise in the red blood cell count and hemoglobin level produced by the folic acid, when the erythrocyte count was greater than 3,000,000. In this case, unlike some of the other cases reported in which folic acid alone was administered, the response was maximal and sustained. The end result of this combination of folic acid, stomach extract and iron and sodium citrate was an entirely satisfactory increase in the number of erythrocytes to above 4,000,000 and in the production of hemoglobin to more than 13 Gm. per hundred cubic centimeters. It is noteworthy that the macrocytosis has persisted. The patient is now living a normal life and is free of those symptoms which were responsible for bringing her under observation. It is unlikely that liver extract, if tolerated, would have produced a more perfect result. It is probable that the disease would have terminated fatally had not treatment with folic acid and dried stomach been used.

SUMMARY

1. A case of macrocytic anemia with organ-specific allergy to liver extract is reported.

2. Administration of folic acid followed later by that of dried stomach and iron solved the serious problem of persistent allergy to liver extract and resulted in maximal and prolonged maturation of erythrocytes.

ADDITIONAL NOTE: The blood values after seven months of continuous medication with the same dosage were as follows: red blood cells, 4.25 million; hemoglobin, 12.75 Gm. per hundred cubic centimeters, and mean corpuscular volume, 90 cubic microns.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

THEOPHYLLINE ETHYLENEDIAMINE (See New and Nonofficial Remedies, 1946, p. 395).

The following dosage forms have been accepted:

H. E. DUBIN LABORATORIES, INC., NEW YORK

Aminophylline (Powder): 15 Gm., 113 Gm., and 454 Gm. bottles.

PREMO PHARMACEUTICAL LABORATORIES, INC., NEW YORK

Aminophylline (Powder): 28.35 Gm. and 113.39 Gm. bottles.

Tablets Aminophylline: 0.1 Gm. and 0.2 Gm.

Enerals Aminophylline: 0.2 Gm. Each tablet is enteric coated with a shellac-castor oil mixture.

Solution Aminophylline: Ampuls 0.25 Gm. in 10 cc. and 0.5 Gm. in 2 cc.

ZEPHIRAN CHLORIDE (See New and Nonofficial Remedies, 1946, p. 113).

The following additional dosage form has been accepted:

WINTHROP CHEMICAL CO., INC., NEW YORK

Zephiran Chloride Solution (Concentrate) 12.8%: 118 cc. and 3.79 liter bottles. A concentrated solution of Zephiran Chloride which may be diluted with water or isotonic salt solution before use.

Zephiran Tint: 1.81 Gm. vials, D and C red No. 39, for use in the preparation of colored Zephiran Chloride Solutions.

METHENAMINE (See New and Nonofficial Remedies, 1946, p. 176).

The following dosage form has been accepted:

E. S. MILLER LABORATORIES, INC., LOS ANGELES

Tablets Methenamine: 0.3 Gm.

SULFADIAZINE (See New and Nonofficial Remedies, 1946, p. 181).

The following dosage form has been accepted:

E. S. MILLER LABORATORIES, INC., LOS ANGELES

Tablets Sulfadiazine: 0.5 Gm.

MANNITOL HEXANITRATE (See New and Nonofficial Remedies, 1946, p. 336).

The following dosage form has been accepted:

THE SMITH-DORSEY COMPANY, LINCOLN, NEB.

Tablets Mannitol Hexanitrate: 30 mg.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JANUARY 18, 1947

PLANNING FOR HEALTH

On January 3 Hon. Robert A. Taft, senator from Ohio, spoke over the facilities of the National Broadcasting Company on "A Republican Program." In the course of the address, which appeared later as "Extension of Remarks" in the *Congressional Record,* Senator Taft referred briefly to the place of health in the program. He said:

> So also in the health field we are proposing a program to assist the states and local governments in making their treatment of the indigent and medically indigent more systematic and complete. We should encourage the formation of plans for voluntary health insurance to be available to those who wish to take it out. On the other hand, we strenuously oppose the Wagner-Murray-Dingell bill, which attempts to impose a complete system of compulsory sickness insurance on all the people in the United States. That plan would tax the people to raise four or five billion dollars a year to pour into Washington to be used by a federal bureau to pay all the doctors to give free medical care to all the people of the United States. It is not only a socialization of medicine but it is the federalization of medicine. No other measure before the American people proposes such a tremendous increase in the right of the federal government to interfere with the daily lives of the people. It flies in the face of every principle for which the Republican Party stands.

The language is direct; the principles are sound; the message is heartening!

In his message to the Congress on the state of the nation, President Truman indicated in vague generalities his belief in the desirability of better availability for medical care. Then on January 10 he sent to the Congress his budget and his message, in which he was somewhat more explicit. He said:

> Recent legislation for hospital construction, for increased activities in mental health and for expanded maternal and child health services are substantial achievements toward improving the substandard health level of a large part of the population. But the major problem of financing health care still persists. Therefore I again urge the Congress to enact a health insurance program which will make adequate medical care available to every one and provide protection against the economic hardships of sickness. Such a program should be almost entirely self financing through payroll contributions.

Last year the President carefully explained several times that he did not believe this program to be "socialized medicine." That excursion into semantics was of little avail in convincing the American people. Now taxes are referred to pleasantly as "payroll contributions." Moreover, the medical care of all the people by a bureaucracy is characterized as "health insurance." Isn't it really "federalized medicine"?

On January 10 also Senator J. William Fulbright, Democrat of Arkansas, for himself and Senator Robert A. Taft, Republican of Ohio, introduced a proposal for a new Department of Health, Education and Security in the Cabinet. This proposal would put all health, social security and educational functions of the government under supervision of a new Cabinet officer. Already conferences are being developed in which representatives of various national organizations concerned with these functions in our civilization will meet to interchange views on the principles which should prevail in the establishment of such an agency and on the qualifications of the personnel selected to administer the services. The proposal would seem to be a much needed step toward assembling the medical functions of the federal government in a single agency with direct access to the Cabinet. This is a principle for which the American Medical Association has contended since its organization one hundred years ago. The fact that President Truman suggested its adoption in his message this year and that the proposal comes under joint sponsorship of both major political parties would seem to indicate likelihood of early enactment.

In his message President Truman referred also to the desirability of legislation in behalf of the establishment of a National Science Foundation. At a recent meeting of the American Association for the Advancement of Science, leaders in many fields of science, including medicine, proposed early conferences with a view to improving on the text of the Kilgore-Magnuson bill, which passed the Senate last year. On this subject Senator Taft said recently:

> We are also proposing a measure to set up a permanent scientific foundation to promote research in many fields. Our measure creates a scientific council of fifty leading scientists to select the director and determine the scope of the work. This is a substantial modification of the Kilgore-Magnuson bill of the last session, which authorized the President to appoint a director with fifteen bureau chiefs and an elaborate organization, directly subject to political pressure.

Here again there would appear to be a desire to give government back to the people!

In concluding his message Senator Taft said:

> In every field they will invite counsel from the best minds, initiate studies and recommend measures for future enactment.

Physicians who have fought unceasingly in behalf of the fundamental principles of freedom in the intimate affairs of our lives and in the further advancement of medical science, which has reached, under our system of government, the highest level ever attained anywhere in the world, will read in these words a promise of success for our objectives. Physicians know the importance of unimpeded respiration for health and vitality. Apparently we may—at least for a time—breathe easier.

VAGOTOMY FOR PEPTIC ULCER

Animal experiments in which a Pavlov or Heidenhain pouch was utilized have demonstrated that pure gastric juice has an aggressive action on living tissue as contrasted with that of the usual gastric content. The composition of the material in the stomach is usually a mixture of swallowed food and saliva, gastric juices from the parietal cells of the fundus, a mucous and a neutral or faintly alkaline secretion from the pyloric antrum and varying quantities of regurgitated duodenal juices. This material is relatively inert. Carlson demonstrated that a continuous gastric secretion occurs which is not dependent on the presence of food. Its small volume permits its neutralization by the mucus of the pyloric antrum, swallowed saliva and possibly also regurgitated duodenal contents. Dragstedt [1] suggests that this neutralizing mechanism may fail or prove inadequate and that, as a result, more or less pure gastric juice may accumulate in a stomach empty of food. Artificially induced, continued excessive secretion of gastric juice following implantation of histamine pellets in wax produced ulcers in all the common laboratory animals.

Acting on the concept that the hypersecretion of gastric juice in gastroduodenal ulcer is largely neurogenic, Dragstedt treated a series of patients who were troubled with more or less intractable gastroduodenal ulceration by utilizing an operation designed to remove permanently and as completely as possible the vagus innervation of the stomach. Incomplete vagotomies performed in the past (Weinstein, Winkelstein) have not been followed by a beneficial therapeutic effect. The desirability of a complete vagotomy was indicated by the studies of Hartzell, who demonstrated in dogs that section of both nerves decreases the acidity of the gastric contents. If the section is technically incomplete, the effect is disappointing. Experiments confirming and extending these observations were performed by Dragstedt and his associates on animals with totally isolated stomachs, both with and without vagal innervation.

Thornton, Storer and Dragstedt,[2] in reporting the results of intrathoracic vagotomy on 38 patients with duodenal, gastric or gastrojejunal ulcer, state that the postoperative course indicated complete relief of ulcer symptoms, objective evidence of healing of the ulcers and definite improvement in general health in almost all. The average twelve hour continuous secretion obtained in 8 patients with duodenal ulcers and in 2 patients with gastric ulcers before the vagotomy amounted to 821 cc., and this decreased to 335 cc. after division of the vagus nerves. The free acidity was 47 clinical units before and fell to 15 units after the operation. Histamine stimulation produced an abundant secretion of acid gastric juice in 19 patients thus tested before operation, and there was no diminution either in volume or in free acidity after the vagus section. This lack of response parallels the experiments on animals and is explained by the fact that histamine acts on the peripheral neuroglandular apparatus or directly on the secreting cells and not through the mediation of the vagi. Of 15 patients submitted to the insulin test, 14 were not affected by insulin following vagotomy. A decrease in the gastric tonus and in the frequency and amplitude of the hunger contractions was present in each case.

Excessive, continuous secretion of gastric juice occurs in most patients with gastroduodenal ulcer in the absence of any known type of gastric secretory stimulus. The reduction in this secretion produced by complete division of the vagus nerves to the stomach proves that the hypersecretion is neurogenic in character. The most pronounced and regular departure in these cases from the normal lies in the volume and acidity of the continuous night secretion. This is apt to be especially large in young people with duodenal ulcer who present in varying degree other signs of nervous tension and instability.

Grimson [3] subjected 18 patients with refractory ulcers that had produced serious symptoms during an average time of eleven years to intrathoracic vagotomy. The ulcers healed in several weeks. Twelve hour night secretion volumes were reduced from an average of 946 cc. before operation to an average of 342 cc. after operation. The acidity of the secretion of the fasting stomach was changed from an average p_H of 1.72 before operation to an average of 3.55 afterward. Insulin hypoglycemia produced an average maximum increase of free acid to 105 cc. before operation and to 23 cc. several weeks and several months afterward. Gastrometric examination revealed a remarkable reduction to subnormal of the gastric hypermotility observed before operation.

Fifteen patients were selected by Moore and his associates [4] because of the long duration and intractability of the symptoms of intractable peptic ulcer as well as the past and present complications. All the patients had had one or more rigorous terms of hospital medical treatment. Following transthoracic vagotomy the patients were allowed to eat and drink anything they wished, including alcohol and coffee, since it was believed that the operation would not be put to an adequate test if the patient continued rigid medical therapy. The ulcers of 12 patients have healed or are healing, and all but 1 patient had immediate and

1. Dragstedt, L. R.: Pathogenesis of Gastroduodenal Ulcer, Arch. Surg. **44**: 438 (March) 1942.

2. Thornton, T. F., Jr.; Storer, E. H., and Dragstedt, L. R.: Supradiaphragmatic Section of the Vagus Nerves, J. A. M. A. **130**: 764 (March 23) 1946.

3. Grimson, K. S., in discussion on preceding paper, p. 769.

4. Moore, F. D.; Chapman, W. P.; Schulz, M. D., and Jones, C. M.: Transdiaphragmatic Resection of the Vagus Nerves for Peptic Ulcer, New England J. Med. **234**: 241 (Feb. 21) 1946.

sustained symptomatic relief. There have been no surgical complications such as empyema, persistent pneumothorax or cardiospasm. This procedure is particularly applicable, in the opinion of these authors, to patients who have had other surgical interventions, such as pyloroplasty, posterior gastrojejunostomy or gastric resection and who present themselves with renewed ulceration. The largest group in which this procedure seems of value are young or middle aged patients with a long history of peptic ulceration, possibly with previous perforations or hemorrhages, unobstructed and not acutely bleeding, who have been refractory to medical treatment and who have severe ulcer pain in times of stress, which can be relieved transiently by the usual antiacid, milk or food. The operation is contraindicated in acute perforation, acute massive hemorrhage or advanced cicatricial obstruction.

The period of observation has been too short to permit a final evaluation of the method, and the question of ultimate regeneration of the divided vagi remains undecided. Such complications as dilatation of the stomach and greatly impaired motility make necessary delay in final conclusions regarding the exact value of the technic.

WATCH THE ANTIVIVISECTIONISTS

State legislators are meeting in 1947 in forty-four states. In some of these legislatures bills will be introduced by the antivivisectionists seeking curtailment of the use of animals in research. The possible crippling of medical progress, medical education, manufacture of pharmaceuticals and standardization of drugs for therapeutic use as a result of their efforts does not concern the antivivisectionists. Unless they are effectively inhibited they may come even more perilously close to success than they did in the legislative session in New York when their dog bill passed one house of the legislature. Only the vigilance of New York physicians and scientists succeeded in stopping them.

The annual report [1] of the National Anti-Vivisection Society, 37 South Wabash Avenue, Chicago, contains a copy of a letter which is being sent to approximately 13,000 state legislators individually typed and signed by Ward Caille, the vice president. Accompanying the letter will be a postcard, return envelop and a copy of a booklet, "The Case Against Vivisection," which is an alleged refutation of a powerful article in *Collier's*,[2] which established beyond doubt the necessity for using animals in research.

In this letter there is the usual medley of misstatements. Claim is made that in the membership of the National Anti-Vivisection Society "there is a percentage of licensed physicians ten times greater than the percentage of physicians in the whole American population, and for reasons they well understand only a few of these doctors deem it wise to allow us the use of their names." This is statistical hocus-pocus which tells exactly nothing; the membership rolls of the National Anti-Vivisection Society have never been open to inspection.

The Anti-Vivisectionists' letter admits that "torture of animals" can exist only by nonenforcement of anti-cruelty laws but does not explain the persistent reluctance of the antivivisection societies to invoke such laws, nor does it mention the ignominious court reverse sustained by them in Chicago on one of the few occasions when they were unwise enough to venture into prosecution.

The letter pretends "we need to know for our own guidance how legislators as a class feel" and "legislators are second only to doctors in their importance and interest to us." It closes with a request for a personal favor to check the "enclosed card and seal it in the enclosed return envelop. As pointed out above, your signature is entirely optional." Following is a reproduction of the card:

> I am (for) (against) the vivisection of animals.
>
> IF "AGAINST," PLEASE GO ON TO CHECK ONE OR MORE OF THE STATEMENTS BELOW
>
> ☐ Unfortunately, I would not vote for anti-vivisection legislation now because I feel such action would be premature.
>
> ☐ I would support anti-vivisection legislation with my vote, at present, but only with my vote.
>
> ☐ I would support anti-vivisection legislation by both my vote and the influence of my publicly expressed opinion.
>
> ☐ I would support anti-vivisection legislation by any means, deeming it right and considering it important enough not to be submerged by other political problems.

This is an old dodge in a new dress. It was tried on the medical profession some years ago. Questionnaires sent to physicians resulted in approximately 3,600 replies, which represents just about 5 per cent of the profession. In this 5 per cent would naturally be included all the proponents of the antivivisectionist movement, but even so these constituted only a bare majority of physicians replying. Nevertheless this so-called "poll" has been widely quoted as an indication that doctors favor the activities of the antivivisectionists against medical research.

This legislative poll, it may safely be predicted, will be used as the medical poll was used. No matter how small the number of legislators who reply, the proponents will quite likely constitute a majority, since most recipients of the questionnaire will file it in the waste-basket. The false "majority" thus engineered by questionable statistical practices will be widely publicized as representing the "attitude of legislators" toward antivivisectionists.

1. Annual Report, National Anti-Vivisection Society, Dec. 31, 1946.
2. Kirk, N. T., and Ratcliff, J. D.: Mice or Men? Collier's, June 29, 1946.

The antivivisectionists distributed over 2,000,000 pieces of literature in 1946. "Every state in the Union was covered and in some instances entire towns were blanketed." They have lists of dog licenses, and their members send them names copied from local telephone books.

Unless the medical profession and allied scientists and educators are alert we may yet see science humiliated by the enactment of crackbrained legislation.

Current Comment

1,646 SUCCESSFUL VACCINATIONS ON A TROOP SHIP

Ten days out from Suez on a troopship bound for New Zealand,[1] a man was admitted to the hospital with a diagnosis of acute tonsillitis. Two days later a papular rash appeared; on the following day the rash increased with a tendency to coalesce over the face, shoulder, upper arm and other areas. Next day the papules showed gray-white tops; some were umbilicated, and there was further coalescence. The patient now was drowsy and confused. The eruption progressed until only five small areas of clear skin remained through which to pass a hypodermic needle. At a consultation of medical officers on board, on the fifth day, the consensus was that this was a case of smallpox. On the twelfth day the patient died. Vaccination scars were not found on his skin. He had never been successfully vaccinated in the Army. Investigation showed that he had been A. W. O. L. before embarkation and had been picked up in the most doubtful part of an out of bounds area. When smallpox was suspected, all contacts were vaccinated and the ship's company was revaccinated. The amazing result was a total of 1,646 successful vaccinations. Precautions taken to prevent the introduction of smallpox into Australia, where some of the troops disembarked, and into New Zealand apparently were adequate. Palmer states that the population in New Zealand is virtually unprotected. Its medical practitioners, however, fully realize, as physicians do everywhere, that successful vaccination is the only sure means of preventing an outbreak of smallpox. If their fellow countrymen also were convinced, public opinion would force army authorities to see that their soldiers were immunized against this disfiguring and often fatal disease. A few cases of serious and even fatal smallpox occurred in the United States Army during the recent war. These are believed to have been due, however, not to failure to vaccinate but to failure to vaccinate properly and to interpret the results correctly. Now comes a recent report that 820 cases of smallpox occurred in Hong Kong in November and that 530 cases were fatal. Civilians should be urged to have successful vaccination against smallpox. The hazard is especially important for those who travel.

1. Palmer, G. B.: Confluent Smallpox; Report of a Case, New Zealand M. J. 45:249 (Oct.) 1946.

EUPHEMISMS AND EQUIVALENTS IN TEACHING AND PRACTICE

While the education of the public in medical matters is desirable, certain factors inevitably associated with the process produce undesirable effects, particularly in neurotic and suggestible persons. The increasing flow of medical information given to the public through the press and the radio makes persons aware of the seriousness of certain diseases and arouses dread in the apprehensive that they may become victims of some of these conditions. If this leads, as it frequently does, to prompt consultation with a physician when dubious symptoms arise, the effect is highly desirable. Unfortunately, unduly apprehensive people may not be reassured even by a favorable report, and others often fail to consult a physician. The printed page and the radio broadcast are not the only, or even the chief, sources of education of the public in medical matters. The physician, both as practitioner and as teacher, bears a heavy responsibility in this field. The treatment of many diseases is much more efficient when the patient is informed of the underlying principles. However, in the instruction of patients discretion and tact on the part of the physician are essential. The use of terms which are ominous or even terrifying must be avoided. This is best done by the use of euphemisms, which the dictionary defines as "mild or agreeable expressions for something disagreeable." The teacher of medicine, particularly in bedside instruction, is in a position to do considerable harm if he fails to select his language with care. It is customary on teaching rounds and in bedside clinics for a student to recount the history of the patient. If this is not done intelligently a nervous patient may be frightened almost out of his senses. In the subsidiary questioning too both the questions and the answers should avoid terms which are of grave import to the average layman. After the history has been elicited and the pertinent observations have been demonstrated, the diagnosis should not be discussed before the patient. Medical students must be instructed in the principles discussed and must be given a working knowledge of the use of euphemisms and equivalents. Patients with a history of syphilis may be reported as luetics, those having positive Wassermann tests may be described as having positive complement fixation tests. In cases of angina pectoris the disease may be discussed with students in the presence of the patient as stenocardia. Patients with this disease may be told that they are suffering from spasm of the heart arteries or attacks of anoxemia of the heart muscle. In like manner neoplasm, without the qualifying adjective malignant, may be used to describe carcinomas and other growths. Excessive addiction to alcohol may be spoken of as ethylism. These are but a few examples of the many euphemisms or equivalents that may be used. This whole question is bound with the ancient but newly stressed conception of disease as involving not only the soma but the psyche, an idea not usually grasped in its full implication by the medical tyro but borne in on the practitioner with cumulative force as his experience increases.

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

Jan. 13, 1947.

President Asks for Broadened Health Program and Social Security

President Truman informed the Republican 80th Congress in his state of the Union message of his labor proposals and desire for cooperation. His legislative plans contained a comprehensive national health program and broadened social security. Mr. Truman also advocated the creation of a Department of Welfare to handle health, education and welfare. "Of all our national resources," he stated, "none is of more basic value than the health of our people. Over a year ago I presented to the Congress my views on a national health program. The Congress acted on several of the recommendations of this program—mental health, the health of mothers and children and hospital construction. I urge the Congress to complete the work begun last year and to enact the most important recommendation of the program—to provide adequate medical care for all who need it, not as charity, but on the basis of payments made by the beneficiaries of the program."

Physician Veterans Want Hospitals to Employ Doctors with Military Service

The Physician Veterans of World War II, known here as the "Docvets," protested to the Surgeons General of the Army and Navy against a deferment policy whereby recent medical graduates can obtain a deferment if they present letters from hospitals saying they have jobs as residents. A spokesman said "We believe such jobs should go to competent physician veterans." Navy Surgeon General Swanson promised that no deferment because of hospital residency would be granted if a physician veteran can take the job. Army Surgeon General Kirk explained that 3,000 medical school graduates whose tuition was paid by the government are available for army service. The Army can't use them now, which is the reason for deferments. The Docvets applauded General Kirk's comment that hospitals should employ veterans rather than younger doctors without military service.

Rh Blood Laboratory Set Up in Capital

Two doctors who served in the Army Medical Corps during the war in laboratory blood testing and blood bank work plan are setting up a central laboratory to make Rh blood available to Washington mothers. They are Dr. Oscar B. Hunter Jr., son of Dr. Oscar B. Hunter, secretary-treasurer of Doctors Hospital and a governor of the new Congress of American Pathology, and Dr. John Ross, son of Charles G. Ross, White House press secretary.

Representative Lemke Revives Bill to Outlaw Vivisection

Representative Lemke, Republican of North Dakota, has reintroduced his bill to outlaw medical experiments on living dogs in the District of Columbia. The measure has been defeated in past sessions. The bill would make it a misdemeanor to experiment or to perform any operation on living dogs except those normally performed for the convenience of the owner and "welfare and curing" of the animal. The bill was referred to the House District Committee.

Health and Welfare Stressed in Economic Report

In his economic report to Congress, President Truman advocated increased old age benefits and survivors' insurance under Social Security and extended aids to the blind and dependent children beyond 1947. The boost in Social Security benefits was asked to meet rising living costs. Also recommended was long range revision of social security laws to increase the amount and duration of unemployment benefits, sickness and disability insurance for workers and partial federal financing of the Social Security system. Mr. Truman said "Health insurance relates clearly to the efficiency of workers and thus to the productivity of industry and agriculture. And this is even true of education, which must be reshaped continuously to meet the changing demands and job opportunities of the machine age or, some day, of the atomic age."

National Health Insurance Law Slated for Consideration by New Congress

Senator Smith, Republican of New Jersey, announced that he would launch a Republican drive for enactment of a national health insurance law early in the new Congress. His plan would provide voluntary participation, with each state to work out its own insurance program for hospital and medical care. He advocates a $200 million federal fund from which aid could be supplied to help low income groups. The proposal differs considerably from the administration's compulsory insurance plan which failed to win enactment at the last session. "We want to give the greatest measure of freedom to the states in setting up their health insurance plans," explained Senator Smith. His bill would create a council to which a state could appeal any dispute over proposed grants-in-aid, which would be on the basis of $2 in federal funds for every $1 paid by the state. Senator Smith is on the committee which will report on a health program for the Senate Republican members.

Swedish Hospital Is Model for Washington's New Hospital Center

W. E. Reynolds, U. S. public buildings administrator, has returned from a European trip with enthusiastic reports about Stockholm's new Soder Hospital, built during the war, which is said to be the only permanent, modern and complete hospital equipped for all specialties of medicine. It has been suggested as a model for the $20 million hospital center. The Stockholm plan, if adopted, would have to be modified to conform to the fact that Emergency, Garfield and Episcopal hospitals, to be merged in the new center, must maintain their identities to preserve endowments and other assets. The Stockholm hospital is municipally owned and has small emergency receiving stations located in large areas. Planes, ambulances, motorboats and trains are used to speed patients needing specialized treatment to large hospitals.

President Comments on Need for Continued Research and Patents

President Truman explained in his Economic Report his recent action to stimulate research, stating "The United States will this year invest more than a billion dollars in research. In order to protect national security and the development of the domestic economy I have established by executive order a presidential research board to survey federal research and development programs. The continuation of a research program of large magnitude for many years to come, together with the fact that many of the inventions resulting from it will be patentable, calls for action to protect the public interest in inventions and discoveries resulting from expenditures of public funds."

National Science Foundation Nearer Reality by Boston Resolution

Advocates of a National Science Foundation believe that this project is nearer realization than ever before as a result of the resolution adopted by the policy council of the American Association for the Advancement of Science in Boston. An intersociety committee was formed to press for legislation to create such a foundation. Dr. Kirtley F. Mather, chairman of the committee, and Dr. Harlow Shapley, new president of the association, stated that the Kilgore-Magnuson bill, passed last year by the Senate only to die in House committee,

would be satisfactory if enacted by the 80th Congress. The resolution stated that "the creation of a National Science Foundation to support fundamental scientific research and the education of scientists is of utmost importance for the health, security and welfare of the nation."

Liberated Japan Adopting Startling Program of Eugenics

Copies of the *Nippon Times* of Tokyo of November 6 reaching Washington officials reveal that liberated Japan, through its Population Policy Commission, is about to adopt a program of eugenics which American newspaper commentators say bears resemblance to programs enforced by Hitler. The Japanese plan makes no mention of Nordics or non-Nordics but refers to "qualified" and "unqualified" parents. For the latter, sterilization and compulsory castration are proposed. Another feature "to control births and produce a better race" includes abortion "to protect the health of the mother or for ethical reasons, such as "conception due to rape, error or ignorance."

War Department Seeks Adoption of Universal Military Training

Although President Truman has advocated dropping the word "military" from his proposed program of national youth training, the War Department will endeavor to have this economy minded Congress adopt its program of universal military training. An official statement points out that the whole cost of universal military program for one year would cost less than three days of the second world war, $800 million. The War Department points out that a civilian commission would control the program, which would emphasize physical and religious development.

Dr. Albert F. Woods to Continue Research in Plant Disease Viruses

On his retirement December 31 as educational adviser of the Department of Agriculture, Dr. Albert F. Woods, a veteran of fifty years with the department, plans to resume research into plant disease viruses which he began in 1895. He is working on the theory of William Stanley, discoverer of the tobacco mosaic virus, that such entities are chemical rather than organic. His research would bear on why certain virus diseases do not yield to drugs, as do bacteria. It is pointed out that there is a close link between viruses and certain types of cancer, such as skin cancer.

Creation Urged of Single Department of National Defense

Merger of the armed forces, long contested in Congress, is on the agenda of the 80th Congress for further consideration. President Truman in his message advocated a single Department of National Defense to cut costs and enhance national security. He also appealed for universal training to develop a trained citizens' reserve. The President also called for extension of Selective Service only if the War Department finds that it is necessary to maintain the strength of the army. The War Department is to report in time for Congress to act. Present draft laws expire March 31.

Senator Langer Advocates Maternity Leave for Federal Worker

Senator Langer proposes to introduce a bill granting women who have at least one year's federal service the right to maternity leave of sixty days. The bill is being prepared by officials of the Federal Security Agency and the Women's Bureau of the Department of Labor. A similar bill failed to pass Congress last year.

President Truman Appeals for March of Dimes

President Truman asked for national support of the annual March of Dimes, January 15 to 30, to finance the fight against infantile paralysis. He will broadcast to the nation on the night of January 30, the sixty-fifth birthday anniversary of the late President Roosevelt, founder of the National Foundation for Infantile Paralysis.

Dr. Calvin Klopp Is Director of Cancer Prevention Clinic

The first cancer prevention clinic to be opened in the District of Columbia is in the Warwick Cancer Clinic at Garfield Memorial Hospital, in charge of Dr. Calvin Klopp. Findings indicative of cancer will be reported to the subject's family or physician. Dr. Klopp explains that the clinic "will make periodic examinations of well people who want to find out if they have cancer and don't know it."

Dr. Bush Is 1946 Winner of Hoover Medal

Dr. Vannevar Bush, president of the Carnegie Institution of Washington, has been named 1946 winner of the Hoover Medal, one of the coveted honors of the engineering profession. It is the most recent of the many awards and honorary degrees conferred on him.

Navy Nuclear Scientist Named to Presidental Board

Dr. Philip N. Powers, navy nuclear physicist, has been appointed to President Truman's Scientific Board. He will serve as assistant coordinator of scientific personnel.

Medical Legislation

MEDICAL BILLS IN CONGRESS

Department of Health, Education and Security

Senator Fulbright, Arkansas, for himself and Senator Taft, Ohio, has introduced S. 140, a bill to create an executive department of the government to be known as the Department of Health, Education and Security. This legislation would authorize the appointment by the President of three undersecretaries in the department, an undersecretary for health, an undersecretary for education and an undersecretary for security. The undersecretary for health, the bill provides, must be a doctor of medicine licensed to practice medicine and surgery in one of the states or territories of the United States or in the District of Columbia, and will perform such duties concerning health as may be prescribed by the secretary of the department or required by law.

Department of National Health

Representative Miller, Nebraska, has introduced H. R. 605, a bill to establish a Department of National Health at the head of which shall be the secretary of national health, appointed by the President by and with the advice and consent of the Senate. The declared purpose of this legislation is to bring about, so far as practicable, a centralization in the Department of National Health of all activities of the federal government relating to health. The President will be required, as soon as practicable after the enactment of the bill, to transfer by executive order from existing departments, agencies and offices of the government, to the Department of National Health, such agencies and functions as he may determine to be appropriate to carry out the declared purpose.

Coming Medical Meetings

Annual Congress on Medical Education and Licensure, Chicago, Palmer House, Feb. 10-11. Dr. Victor Johnson, 535 N. Dearborn St., Chicago 10, Secretary.

American Academy of Orthopedic Surgeons, Chicago, Jan. 25-30. Dr. Myron O. Henry, 825 Nicollet Ave., Minneapolis, Secretary.

Central Surgical Association, Chicago, Feb. 20-22. Dr. Walter G. Maddock, 250 East Superior St., Chicago, Secretary.

Chicago Medical Society Annual Clinical Conference, Chicago, March 4-7. Dr. Willard O. Thompson, 30 N. Michigan Blvd., Chicago 2, Secretary.

Mid-South Postgraduate Medical Assembly, Memphis, Tenn., Feb. 11-14. Dr. Arthur P. Copper, 1479 Carr Ave., Memphis, Secretary.

New Orleans Graduate Medical Assembly, New Orleans, Feb. 24-27. Dr. Max M. Green, 1430 Tulane Avenue, New Orleans 13, Secretary.

Pacific Coast Surgical Association, Seattle, Feb. 17-18; Victoria, B. C., Feb. 19-21. Dr. F. L. Reichert, Stanford University Hospital, San Francisco, Secretary.

GOVERNMENT SERVICES

ARMY

406th MEDICAL GENERAL LABORATORY IN TOKYO

One of the organizations that assist in safeguarding the health of our occupation forces in Japan is the 406th Medical General Laboratory in Tokyo, which has now been fully staffed and equipped with 20 medical officers, 50 enlisted men, 5 Japanese doctors and 40 Japanese laboratory technicians and helpers. Field teams traveling about Japan in special laboratory cars gather scientific data, which are correlated and interpreted by the laboratory. Some field teams, for example, collect specimens of blood from people and animals in representative areas, as a basis of comparison and further study, in case an outbreak of Japanese B encephalitis should occur. One of the larger projects the laboratory has taken over is the research begun by the Commission on Virus and Rickettsial Diseases on B encephalitis. The laboratory does such routine procedures as examination of surgical tissue removed at operation and various kinds of blood tests. About 5,000 white mice are used each week in the various tests and experimental work. The laboratory analyzes daily the water supply in the Tokyo-Yokohama area and examines certain food products, such as ice cream, used by soldiers throughout Japan. Most of the routine testing of foods and drugs consumed by Allied personnel is carried out in this army installation, which is the only one of its type in Japan. The commanding officer of the laboratory is Lieut. Col. W. D. Tiggertt.

MEDICAL OFFICERS ATTENDING VENEREOLOGY CLASSES

Major Gen. Norman T. Kirk, the Surgeon General, announces that sixteen selected officers of the Army Medical Department have enrolled in the first postwar classes in venereology at a civilian institution opened in December at the University of Pennsylvania. Such courses have become necessary, General Kirk said, to replace those venereal disease specialists who are being separated from the service, and while this abbreviated course "will not give us specialists in venereal disease management, it will be a step in the right direction." These sixteen officers will study at the Institute for the Study of Venereal Disease at the University of Pennsylvania and at the conclusion of the course will return to their stations in army general hospitals. The course is conducted by Dr. John H. Stokes, director of the institute and medical consultant to the Secretary of War through the Surgeon General.

Another class is scheduled to open in January at the University of Southern California, Los Angeles.

ARMY MEDICAL LIBRARY

A permanent office for the Association of Honorary Consultants to the Army Medical Library has been opened in room 26, Library of Congress, Washington, D. C., where all matter pertaining to the association should be sent.

Mr. Scott Adams, formerly chief of the acquisition division of the library, has been appointed acting librarian to replace Mr. Wyllis Wright, who is leaving to become librarian of Williams College, Williamstown, Mass.

CONFERENCE ON VENEREAL DISEASE CONTROL

At a conference on venereal disease control at the New Grand Hotel, Yokohama, Japan, Dec. 4, 1946 opening remarks were presented by Lieut. Gen. Robert L. Eichelberger, commanding general, Eighth Army, and Col. Philip L. Cook, M. C., surgeon, Eighth Army. Col. G. N. Schuhmann, M. C., also of headquarters, Eighth Army, outlined the purpose of the conference. Lieut. Col. J. S. Smith, Inf., commanding officer West Camp, Kobe Base, discussed development of the hospital annex and the method of venereal disease control in use at the base, and Capt. J. E. Harroun, M. C., Surgeon's Office, Yobas, studies of venereal disease in Yobas. Other speakers were Lieut. A. H. Randelman, M. C., venereal disease control officer, and Dr. O. M. Elkins, consultant in venereal disease control, G.Hq. S. C. A. P.

VETERANS ADMINISTRATION

OSTEOPATHS TO SERVE IN VETERANS ADMINISTRATION

The Veterans Administration, Washington, D. C., announces that arrangments have been completed for the appointment of doctors of osteopathy to serve in the Veterans Administration, department of medicine and surgery. The appointments will be made in compliance with Public Law 293 (79th Congress), which authorizes the Veterans Administration to hire doctors of osteopathy to work with veterans. To be eligible a doctor of osteopathy must be a citizen of the United States, hold a degree of osteopathy from a college or university recognized by the Veterans Administration, hold a license to practice osteopathy in one of the states, territories or the District of Columbia, have completed an internship satisfactory to the Veterans Administration, and meet prescribed physical standards.

RESIDENCY TRAINING IN NEUROLOGY

Additional residency training programs for Veterans Administration physicians interested in neurology have been organized. The residencies, which will vary from one to three years, are designed to prepare residents for certification in neurology by the American Board of Psychiatry and Neurology.

One training program will be conducted under the joint auspices of Boston University, Tufts Medical College and Harvard University. Residents will be stationed at the Veterans Administration hospital at Framingham, Mass., which has special units for the study of epilepsy, aphasia, paraplegia and electroencephalography and a complete diagnostic neurologic service. Applications should be sent to Dr. Harry C. Solomon, chairman, Deans Subcommittee for Neuropsychiatry, Harvard Medical School, Boston.

The other training program will be conducted at Jefferson Medical College and Clinic, Philadelphia, under the auspices of the Veterans Administration Philadelphia Deans Committee. Dr. Bernard J. Alpers, professor of neurology at the Jefferson Medical College, will direct the program. Applications should be sent to Dr. Edward A. Strecker, chairman, Deans Subcommittee for Neuropsychiatry, University of Pennsylvania School of Medicine, Philadelphia.

Other medical schools affiliated with the Veterans Administration for residency training in neurology where training programs are already under way, are:

Medical School	VA Hospitals and Clinics	Applications Received by
Cornell University Columbia University	Bronx, N. Y. Hospital	Dean Willard C. Rappleye, 630 W. 168th St., New York
Northwestern University University of Illinois	Hines, Ill., Hospital	Dr. Lewis J. Pollock, Northwestern University, Chicago
University of Minnesota	Minneapolis	Dean Harold S. Diehl, University of Minnesota

PUBLIC HEALTH SERVICE

ORGANIZATION FOR NATIONWIDE MEDICAL RESEARCH

The Congress of the United States has designated the National Advisory Health Council, the National Advisory Cancer Council and the National Advisory Mental Health Council to make recommendations to the Surgeon General, U. S. Public Health Service, regarding means necessary to carry out his responsibilities (Public Law 410 section 301, 78th Congress, and Public Law 487, section 7, 79th Congress) with respect to the use of funds for research. In order to provide these advisory councils with expert advice on applications for research grants, the Public Health Service has organized nineteen special study sections, consisting mostly of civilian scientists, in surgery, pathology, public health methods, pharmacology, tropical diseases, antibiotics, bacteriology, biochemistry and nutrition, cardiovascular diseases, gerontology, hematology, malaria, metabolism and endocrinology, physiology, radiobiology, sanitation, syphilis, virus and rickettsial diseases and dental subjects.

Research projects approved by these councils will receive grants in aid. Applications for grants may be made by schools of medicine, hospitals, public or private institutions and individuals. The plan inaugurated by the Public Health Service calls for complete academic freedom and unrestricted opportunity to carry on productive research.

At a recent meeting of the study Section on Metabolism and Endocrinology, Dr. Joseph H. Barach of the University of Pittsburgh was elected chairman. The other members of this section are:

Dr. Charles H. Best, University of Toronto.
Dr. Jerome Conn, University of Michigan.
Dr. Herbert M. Evans, University of California.
Dr. Roy Hertz, National Institute of Health, Washington, D. C.
Dr. F. D. W. Lukens, University of Pennsylvania.
Capt. W. F. Loftin, United States Navy.
Dr. Alexander Marble, Baker Clinic, Boston.
Col. Charles R. Mueller, United States Army.
Dr. Henry B. Mulholland, University of Virginia.
Dr. Lester J. Palmer, Mason Clinic, Seattle.
Dr. Elaine P. Ralli, New York University.
Dr. Henry T. Ricketts, University of Chicago.
Dr. Randall G. Sprague, Mayo Clinic, Rochester, Minn.
Dr. Cecil Striker, Cincinnati.
Dr. Hugh L. C. Wilkerson, executive secretary, U. S. Public Health Service, Washington, D. C.

STATE AGENCIES TO ADMINISTER HILL-BURTON ACT

Forty-three states and territories have designated agencies to administer the Hospital Survey and Construction Act. According to the U. S. Public Health Service, communities, hospitals and professional groups wishing to participate in the program should direct their inquiries to the appropriate state or territorial agency named in the following list:

Alaska	Territorial Department of Health, Juneau	Dr. C. Earl Albrecht Commissioner of Health
Arizona	State Department of Health Phoenix	Dr. G. F. Manning Supt. of Public Health
Arkansas	State Board of Health Little Rock	Dr. T. T. Ross State Health Officer
California	State Dept. of Public Health San Francisco	Dr. Wilton L. Halverson Director of Public Health
Connecticut	State Department of Health Hartford	Dr. Stanley H. Osborn Commissioner of Health
District of Columbia	D. C. Health Department Washington	Dr. George C. Ruhland District Health Officer
Florida	Florida State Improvement Commission, City Administration Building, Tallahassee	Mr. C. H. Overman Director
Georgia	Georgia Department of Public Health, Atlanta	Dr. T. F. Abercrombie Director of Public Health
Hawaii	Territorial Board of Health Honolulu	Dr. C. L. Wilbar, Jr. President, Board of Health
Idaho	Idaho Dept. of Public Health, Boise	Mr. L. J. Peterson, Acting Administrative Director
Illinois	State Dept. of Public Health, Springfield	Dr. Roland H. Cross Director of Public Health
Indiana	State Board of Health Indianapolis	Dr. Lee E. Burney State Health Commissioner
Iowa	State Dept. of Health Des Moines	Dr. Walter L. Bierring State Comr. of Health
Kansas	State Board of Health Topeka	Dr. F. C. Beelman Sec. & Executive Officer
Kentucky	State Department of Health Louisville	Dr. P. E. Blackerby State Health Commissioner
Louisiana	Health & Hospital Division of the Governor Baton Rouge	Mr. Charles Mitchell Director
Maine	Department of Health and Welfare, State Bureau of Health, Augusta	Dr. Leverett D. Bristol Commissioner of Health and Welfare
Maryland	Maryland State Planning Comm., 104 Equitable Building, Baltimore	Mr. I. Alvin Pasarew Director Mr. Henry P. Irr, Chrmn.
Massachusetts	Mass. Dept. of Public Health, Boston	Dr. Vlado A. Getting, Commissioner of Public Health
Minnesota	Minn. Dept. of Health St. Paul	Dr. A. J. Chesley, Secretary & Executive Officer
Mississippi	Miss. Commission on Hospital Care, 207 Tower Building, Jackson	Dr. D. V. Galloway Executive Director
Missouri	State Division of Health, Bureau of Public Health & Welfare	Dr. R. M. James Director, State Div. of Health
Nebraska	Nebraska Dept. of Health Lincoln	Dr. W. S. Petty Director of Health
Nevada	State Dept. of Health Carson City	Dr. Fred S. Loe State Health Officer
New Jersey	New Jersey State Dept. of Institutions & Agencies Trenton	Mr. Sanford Bates Commissioner
New Mexico	New Mexico Dept. of Public Health, Santa Fe	Dr. James R. Scott Director of Health
New York	New York State Postwar Public Works Planning Commission, New York	Mr. John E. Burton Chairman
North Carolina	N. C. Medical Care Commission P. O. Box 1880 613-615 Commercial Bldg. Raleigh	Mr. James H. Clark Chairman
North Dakota	State Dept. of Health Bismarck	Dr. William M. Smith Acting State Health Officer
Ohio	Ohio Dept. of Health Columbus	Dr. Roger E. Heering State Director of Health
Oklahoma	State Health Department 3400 North Eastern Oklahoma City	Dr. Grady F. Mathews Commissioner of Health
Oregon	State Board of Health Portland	Dr. Harold M. Erickson State Health Officer
Pennsylvania	State Dept. of Welfare Harrisburg	Miss S. M. R. O'Hara Sec. of Welfare
Puerto Rico	Dept. of Health San Juan	Dr. Juan A. Pons Commissioner of Health
South Carolina	State Research, Planning & Development Board Columbus	Mr. Robert M. Cooper Director
South Dakota	State Board of Health Pierre	Dr. Gilbert Cottam, Sup't., State Board of Health
Tennessee	Tennessee Dept. of Public Health, Nashville	Dr. R. H. Hutcheson, Commissioner of Public Health
Texas	State Department of Health Austin	Dr. George W. Cox State Health Officer
Utah	State Department of Health Salt Lake City	Dr. William M. McKay State Health Commissioner
Virginia	Virginia Dept. of Health Richmond	Dr. L. J. Roper State Health Commissioner
Washington	State Dept. of Health Seattle	Dr. Arthur L. Ringle State Director of Health
West Virginia	State Dept. of Health Charleston	Dr. N. H. Dyer State Health Commissioner
Wisconsin	State Board of Health Madison	Dr. Carl N. Neupert State Health Officer

CONFERENCE ON GASTRIC CANCER

The Surgeon General of the U. S. Public Health Service announced a conference held at Billings Hospital, University of Chicago, Dec. 5 and 6, 1946, arranged by the Gastric Cancer Committee of the National Advisory Cancer Council. This was the third large conference on gastric cancer sponsored by the council; the first was held in 1940 at the National Institute of Health, Washington, D. C. The recent conference stressed particularly cancer of the gastrointestinal tract. Speakers were present from various parts of the United States. The chairman of the Gastric Cancer Committee of the National Advisory Cancer Council is Dr. George M. Smith, Yale University, New Haven, Conn. The other members of the committee are Dr. Shields Warren, New England Deaconess Hospital, Boston; Dr. Owen Wangensteen, University of Minnesota, Minneapolis; Dr. Alexander Brunschwig, University of Chicago; Dr. Leonell C. Strong, Yale University; Dr. George T. Pack, Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York; Dr. A. C. Ivy, University of Illinois Medical School, Chicago; Dr. Sherwood Moore, Director, Mallinckrodt Institute of Radiology, St. Louis, and Dr. Mandred W. Comfort, Mayo Clinic, Rochester, Minn.

PHYSICIANS SEPARATED FROM SERVICE

ARMY MEDICAL CORPS OFFICERS RECOMMENDED FOR/OR RELIEVED FROM ACTIVE DUTY

Arkansas

Chipman, Raymond A.....Leachville
Daley, Frank R.....Arkansas
Kolb, James M.....Clarksville
Leming, Howell E.....Fayetteville
Watson, Asa C. Jr.....Little Rock

California

Ballantine, David.....San Francisco
Berg, John A.....Sacramento
Bostwick, Allen E.....Los Angeles
Giannini, Albert P.....Santa Clara
Goodman, Stanley.....San Francisco
Heinz, Richard.....Napa County
Joyce, Milton H.....Los Angeles
Leo, Robert J.....Los Angeles
Marsh, Robert L.....Glendale
Newton, Duane T.....San Francisco
Perlmutter, Louis J.....Los Angeles
Rago, Marco R.....Los Angeles
Rocke, Robert S.....Pasadena
Smith, Jay W.....San Francisco
Steen, Claude E. Jr.....Fullerton
Szukalski, Joseph P.....Pasadena
Telling, Marvin H.....San Bernardino

Colorado

Grundset, Lloyd H.....Denver
Jenkins, Harold D.....Denver
McWilliams, John E....Colorado Springs

District of Columbia

Casella, Joseph V.....Washington
Friedman, Nathan B.....Washington
Shull, Harrison J.....Washington
Viscuse, Ferdinand M.....Washington

Georgia

Jacob, Peyton.....Americus
Limbach, David R.....Atlanta
Wells, Edward D. Jr.....Savannah

Illinois

Dunlevy, Robert E.....Chicago
Eastman, Ward H.....Peoria
Greening, Gershom K.....Springfield
Kammerling, Erwin.....Chicago
Kirkwood, Robert C.....Lawrenceville
Klucikowski, Norbert A.....Chicago
Little, John N.....Evanston

Iowa

Baker, Charles J.....Fort Dodge
Fesenmeyer, Charles R.....Riceville
Finnegan, Joseph V.....Carroll
Gann, Edward Russell.....Sigourney
McGavic, John S.....Ft. Madison
McGilvra, Arthur L.....Maurice
Mathiasen, John W.....Council Bluffs
Myerly, William H.....Emmetsburg
Quirin, Lloyd F.....Marcus
Taber, Rodman E.....Marshalltown

Kansas

Beck, Joseph D.....Atwood
Bowen, Harry J. Jr.....Topeka
Haworth, Kenneth W.....Pratt
Ingber, Nathan G.....Wadsworth
Johnson, Delbert P.....Osawatomie
Jones, Edward S.....Canton
McCoy, Frederick J.....McPherson
Miller, Elden V.....Salina
Murphy, Franklin L.....Anthony
Schulz, Donald P.....Beloit

Maryland

Briele, Henry A.....Baltimore
Currie, Dwight M.....Baltimore
Gibbons, James R.....Baltimore
Keeney, Dan F.....Walkersville
Meade, Forest C.....Hyattsville
Tanenbaum, Solomon.....Baltimore

Massachusetts

Gill, Benjamin F.....Brookline
Jillson, Otis F.....Middleboro
MacKinnon, George L.....Wollaston
Sapareto, Rocco L.....Haverhill
White, Malvin F.....Brookline
Wolf, William.....Mattapan
Worthington, Richard V.....Cochituate

Minnesota

Anderson, Harold J.....St. Paul
Nelson, Alfred S.....South Minneapolis

Missouri

Capsey, Roswell E.....Kansas City
Goldman, Melvin L.....St. Louis
Neville, Eugene D.....Clinton

Nebraska

Hermann, Harland T.....Lincoln
Inda, Frank A.....Omaha
Ingham, Charles G.....Wayne
Mattson, Harold A.....Kearney
Morris, Haskell.....Omaha
Neligh, Gordon L. Jr.....Grand Island
Peterson, Stanley S.....Tremont
Peterson, Wendell C.....Fairbury
Raines, Max M.....Weeping Water
Wanek, Frank W.....Aurora

New Hampshire

MacAllister, John D.....Keene
Tanzer, Radford C.....Hanover
Trapp, Harry E. Jr.....Laconia

New Jersey

Kamens, Leslie.....Newark
Reinhart, Harry A.....Atlantic City
Steinhardt, Edward E.....Atlantic City

New York

Andres, Francis A.....Allegany
Anz, Umbert E.....Endicott
Aragon, Potenciano R.....New York
Barney, Bernard B.....Schenectady
Baron, George J.....Rochester
Beamer, George D.....Brooklyn
Bucky, Thomas L.....New York
DeAngelis, Anthony M.....Yonkers
DePue, David D.....Canton
Dinerman, Benjamin.....Brooklyn
Feinblatt, Theodore M.....Brooklyn
Fuchs, George F.....New York
Garben, Louis F. Jr.....Islip
Hubert, James W.....Jamaica
Huggins, Cecil R. Jr.....Andes
Iandoli, Louis J.....Jamaica
Jakobsons, Henry..Richmond Hill, L. I.
Jampol, Morris L.....Brooklyn
Kean, Benjamin H.....New York
King, William E.....Elmhurst
Kirkland, Henry B.....New York
Klebanoff, Milton.....Yonkers
Mellisy, Andrew.....Elmhurst
Milford, Charles R.....Skaneateles
Minkel, Amos J. Jr.....Hamburg
Peters, Nicholas S.....Utica
Pomerantz, Norman.....Albany
Prancl, William J.....Long Island City
Radice, Lawrence J.....Buffalo
Robertson, Douglas H.....Mount Vernon
Schwarz, Eugene E.....New York
Seccafico, Joseph A.....Brooklyn
Sermak, Edmund R.....Olean
Shechtman, Michael.....Bronx
Stockhammer, Stanley F.....Bayside
Stone, William Jr.....New York
Sussman, Harry.....New York
Szoo, Joseph F.....New York
Weisz, Albert B.....Brooklyn
Williams, Selden T. Jr.....Bellerose
Willner, Andre E.....Brooklyn
Winant, Edward M.....New York
Zuckerman, Arthur D.....Brooklyn

North Carolina

Allen, Jerry H. Jr.....Reidsville
Corbin, George W. Jr.....Durham
Daniel, Thomas B.....Oxford
Hawfield, Harold H.....Concord
Lea, Melvin E.....Greensboro
McManus, Hugh F. Jr.....Raleigh
Perry, Glen G.....High Point
Scott, Alan F.....Goldsboro
Smart, Gardner F.....Ayden
Stancil, James R.....Ridgecrest

North Dakota

Clark, Ira D.....Milnor
Kremer, Leslie A.....Linton
Spear, Will N.....Dickinson

Ohio

Buente, Louis C. Jr.....Cincinnati
Imburgia, Frank J.....Cleveland
Jacobs, Donald L.....Cheviot
Kauffman, James R.....Columbus
Mullally, Pierce H. Jr.....Cleveland
Rothe, William S.....Columbus

Oklahoma

Appleton, Meredith M.....Oklahoma City
Batchelor, John J.....Oklahoma City
Binder, Harold J.....Oklahoma City
Box, Otho H. Jr.....Grandfield
Clark, Benjamin P.....Okeene
Kite, William C. Jr.....Oklahoma City
McDonald Glen W.....Binger
Swisher, Forrest M.....Oklahoma City

Pennsylvania

Bean, Carl B.....Meadville
Brobst, Henry T.....Wilkes-Barre
Costello, Patrick J.....Vandling
Machover, Saul.....Pittsburgh
MacLean, Paul D.....Philadelphia
Penta, John J.....Reading
Perry, Joseph H. III.....Rosemont
Raffensperger, E. C.....Boiling Springs
Schnabel, Truman G. Jr.....Philadelphia
Wright, Alfred E.....Uniontown

Rhode Island

Buxton, Bertram H. Jr.....Providence
Coren, Simon.....Providence
DiClemente, Bruno.....Providence
Medoff, Edward B.....Woonsocket
Tartaglino, Eugene J.....Newport

South Carolina

Andrews, Charles H. Jr.....Sumter
Brown, Robert A. Jr.....Greenville
Lee, Frank B.....Scranton
Tanner, Waitus O.....Columbia
Townsend, William B.....Charleston

South Dakota

Reagan, Paul C.....Sioux Falls
Stueland, Alvin J. R.....Sioux Falls

Texas

Bessire, Milton C.....Hamlin
Brucer, Marshall H.....Galveston
East, Norman R.....Houston

Virginia

Armistead, George C. Jr.....Roanoke
Barnes, Robert H. Jr.....Richmond
Bastien, Henry L.....Arlington
Carmines, Fay A.....Odd
DeVito, Michael P.....Alexandria
Jeter, Norbourne B.....Covington
Richards, Ashby T.....Harrisonburg
Walsh, Charles M. III.....Crewe

Puerto Rico

Bertran, Juan M. Jr.....Santurce
Diaz, Luis A.....Rio Piedras
Rodriquez, Ervin Edi.....Ponce

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARIZONA

Arnold B. Kurlander Leaves State Health Department.—Dr. Arnold B. Kurlander, Phoenix, for more than a year director of the mass chest x-ray program of the state department of health's division of tuberculosis control, left recently for Ohio, where he will activate a similar program. Lent to the state by the U. S. Public Health Service, he is credited with doing much to make the people of Arizona conscious of their greatest health problem—tuberculosis. Principal objectives of the survey have been, first, to discover early cases of tuberculosis so that they may be brought under proper medical care and supervision during the most infectious stage of the disease; second, to discover "hidden" cases and assist in their isolation and, third, to educate the people in the problem of tuberculosis. Since late in 1945, when the program began, 108,000 x-ray pictures have been taken, 1,500 of which showed evidence of reinfection pulmonary tuberculosis. The mobile x-ray unit has operated in every county except three, which will be covered in a new series of surveys begun in January of this year.

CALIFORNIA

Herrick Memorial Hospital.—To honor Dr. LeRoy Francis Herrick, who founded the Berkeley Hospital in 1904 and conducted it for twenty-eight years and whose fortune was donated to this community nonprofit enterprise, the board of directors recently dedicated the institution to the founder and named it the Herrick Memorial Hospital. The new $750,000 hospital addition now being completed was financed by a grant and loan from the federal government and is being equipped through contributions and loans from members of the medical staff and friends of the hospital.

Premarital Blood Test Regulations Amended.—The state board of health has amended its regulations, so that hereafter laboratories will not be approved to do antepartum and premarital tests "if they advertise the performance of these tests in magazines, newspapers, directories, circulars, etc., commonly read by the lay public." Laboratories must also submit to check tests and stipulation of the kind of license which must be held by a person who performs antepartum and premarital tests must be made. The new regulations will soon be ready for distribution, according to *California's Health*, a publication of the state department of health.

Midwinter Conferences of Ophthalmology and Otolaryngology.—Guest speakers at the annual midwinter postgraduate clinical conference in ophthalmology and otolaryngology in Los Angeles, January 20-31, sponsored by the Research Study Club, include Drs. Luzius von Rüedi, Bern Switzerland; Sam E. Roberts, Kansas City, Mo.; Samuel Salinger, Chicago; Ben H. Senturia, St. Louis; William L. Benedict, Mayo Clinic, Rochester, Minn.; Henry P. Wagener, Mayo Clinic, Rochester, Minn.; Kenneth C. Swan, Portland, Ore.; David O. Harrington, San Francisco; Dohrmann K. Pischel, San Francisco, and Meyer Wiener, Coronado, Calif.

ILLINOIS

University News.—Gifts and research grants totaling $122,713 have been made to the University of Illinois—$20,000 of which is for the visual education fund of the College of Medicine in Chicago and $16,000 for research in allergy.

Alienists Hold Postgraduate Conference.—Under the anspices of the Division of Alienists, State of Illinois, there will be a two day postgraduate conference in neuropsychiatry at the Lincoln State School and Colony, Lincoln, January 28-29. The speaker of the evening meeting January 28 will be Dr. Anton J. Carlson, emeritus professor of physiology, University of Chicago, whose subject will be "Can research in our state hospitals contribute to the understanding of the causes of alcohol addiction?" Other well known professors and doctors of Illinois will address the sessions.

Illinois Bacteriologists.—At the winter meeting of the Society of Illinois Bacteriologists January 17 Kenneth B. Raper, Ph.D., Peoria, spoke on "Variation in Molds—Natural and Induced." Drs. Katherine E. Hite, H. Close Hesseltine and Louis Goldstein, University of Chicago College of Medicine, presented "A Study of the Bacterial Flora of the Normal and Pathological Vagina and Uterus." Albert Milzer, Ph.D., Chester Byrd and Dr. Sidney O. Levinson, Chicago, reported "The Use of Autolyzed Brain to Facilitate Transmission of Poliomyelitis to Mice." "Factors Influencing the Stability of Influenza Virus" was under discussion by George F. Forster, Ph.D., Venus Love, B.S., and Esther Carson, D.D.S., Illinois Department of Public Health.

Chicago

The Hektoen Lecture.—The twenty-third Ludvig Hektoen Lecture of the Frank Billings Foundation will be delivered at the Palmer House Friday, March 28, at 8 p. m. by Dr. Herbert M. Evans, director, Institute of Experimental Biology, University of California, on "The Internal Secretions of the Pituitary Body."

Personal.—Dr. Lester R. Dragstedt, professor of surgery, University of Chicago School of Medicine, addressed the Baltimore City Medical Society, Baltimore, Dec. 6, 1946 on "Section of the Vagus Nerves to the Stomach in the Treatment of Peptic Ulcer."——Albert Milzer, Ph.D., formerly research virologist of the Samuel Deutsch Serum Center, Chicago, has been appointed director of the department of bacteriology, Michael Reese Hospital, Chicago, to succeed Dr. Katharine M. Howell, who retired Dec. 31, 1946.

Institute of Medicine Elects Officers.—The Institute of Medicine of Chicago has announced that Drs. Joseph L. Baer has been elected president for 1947; William H. Welker, vice president; George H. Coleman, secretary, and Grant H. Laing, treasurer. Dr. William F. Petersen is chairman of the board of governors, and Drs. Joseph L. Baer, Warren H. Cole and LeRoy H. Sloan have been elected governors for terms of five years. Drs. Stanley Gibson and J. Roscoe Miller have been elected to the unexpired terms of Drs. Ludvig Hektoen and James B. Herrick, who because of age have resigned as members of the board after thirty-one years of continuous and exceptional service.

INDIANA

Changes in Health Officers.—Dr. Charles M. Gibbs recently resigned as Greenfield city health officer after serving many years. His successor will be Dr. R. E. Kinneman, Greenfield.

Countywide Immunization.—Through the county medical society free immunization service has been offered to school children throughout the city of Columbus and Bartholomew County in relation to diphtheria, whooping cough and smallpox.

Acting Medical Director of University Medical Center.—Dr. Donald J. Caseley was recently appointed acting medical director of the Indiana University Medical Center, succeeding Dr. John D. Van Nuys. Dr. Caseley, a native of Sullivan, Ill., received his A.B. degree from DePauw University in 1933 and a medical degree from Indiana University School of Medicine in 1937. He interned at Indianapolis City Hospital. He also served as an orthopedic surgeon in the Army Medical Corps in the recent war.

KENTUCKY

Personal.—Dr. Milus L. Gunn, Harlan, has left for India to do specialized study in the Church Missionary Society of England Hospital, Shikapur, India, located near the Iranian border.

Eight Scholarships Established.—Eight scholarships of $2,000 each have been established for the $100,000 Medical Scholarship Fund for medical students who agree to practice in rural districts of Kentucky after graduation. The scholarships will be administered by the trustees of the fund for the Kentucky State Medical Association and the University of Louisville School of Medicine. According to H. Fred Willkie, Louisville, chairman of the General Fund Committee, Dr. Omer Forest Hume, Richmond, donated the first scholarship. Dr. Hume graduated from the medical department of the University of Louisville in 1917. The Dr. Van A. Stilley Memorial Scholarship has been set up by his heirs. The late Dr. Stilley served as field director for the state department of health in western Kentucky and was president of the state medical association in 1943. The Houston Memorial Scholarship has been granted by Mrs. Jesse Houston Roane, Drs. Hugh L. Houston and Hal E. Houston, Murray, in memory of their father, the late Dr. Edward Brent Houston, one of the leading physicians

of Calloway County for thirty years. The scholarship is to be awarded to a premedical student of high standing from Murray State College. Dr. Carl Clifford Howard, Glasgow, present counselor of the association and chairman of the board of trustees of the Medical Scholarship Fund, has presented the Howard Clinic Scholarship. A scholarship was granted by Dr. Gaithel L. Simpson, Greenville, member of the state board of health and board of trustees of the scholarship fund.

Three scholarships of $2,000 each honoring Dr. Charles W. Jefferson, Louisville, have been set up at the University of Louisville School of Medicine by Joseph E. Seagram and Sons Company, distillers, which Dr. Jefferson serves as physician. The Dr. Charles W. Jefferson Scholarship for Surgery was donated by H. Fred Willkie, vice president of the company, and Mrs. Willkie. The Charles W. Jefferson Industrial Medicine Scholarship was raised by employees from cafeteria funds and recreational programs. The Charles W. Jefferson Scholarship for Rural Medicine was established by the company. About one third of the total fund has been subscribed. The revolving Medical Scholarship Fund, launched Dec. 12, 1945, was set up originally as a revolving fund of $50,000 to $75,000 (THE JOURNAL, Jan. 19, 1046, p. 162), and the first scholarship was awarded last spring. The trustees of the fund are Drs. John W. Moore, dean, University of Louisville School of Medicine; Gaithel L. Simpson, Greenville; Carl Norfleet, Somerset; Philip E. Blackerbey, Louisville; Senator Cass Walden, Edmonton; Joe Betts, Louisville *Courier-Journal;* Russell Dyche, London, and Mrs. Charles Shelton, Louisville.

MARYLAND

Dr. Victor F. Cullen Retires.—A dinner in his honor in Baltimore December 31 marked the retirement of Dr. Victor F. Cullen as superintendent of all Maryland tuberculosis sanatoriums. Dr. Cullen graduated from Johns Hopkins University Medical School and while an intern at St. Joseph's Hospital is said to have developed tuberculosis. After two years of care and treatment in a sanatorium he returned to Maryland. According to the governor, Dr. Cullen is "the father of modern tuberculosis work in Maryland." He is also a past president of the National Tuberculosis Association.

NEW JERSEY

New Orthopedic Society.—At a recent meeting in Long Branch the New Jersey Orthopedic Society with nineteen founder members elected Drs. Leopold Szerlip, Newark, president, Harold W. Smith, Orange, vice president, and Raphael R. Goldenberg, Paterson, secretary-treasurer.

Academy of Medicine.—Dr. Stewart G. Wolf Jr., assistant professor of Medicine, Cornell University Medical College, New York, will give an illustrated lecture before the Academy of Medicine of Northern New Jersey January 23 on "Changes in Gastric Function Associated with Varying Emotional States and Life Situations."

NEW YORK

Society News.—Dr. Merton C. Hatch, associate professor of clinical obstetrics, Syracuse University College of Medicine, January 9 addressed the Jefferson County Medical Society on "Prenatal and Postpartum Care."

Qualifications for Local Health Officers Revised.—The state sanitary code relating to the qualifications of grade I local health officers has been amended and became effective in December 1946. Previous grade I requirements are retained as grade I-A but apply only to health officers of cities and counties having a population of more than 100,000. Qualifications prescribed for grade I-B are somewhat lower than former grade I qualifications. Previous requirement of four years' full time experience is reduced to three years and, in the case of combined full time experience and scholastic training, the amount of experience is reduced from two years to one year. Local health officers of cities having a population of 50,000 to 100,000 and health commissioners of counties having a population of 100,000 or less must possess grade I-B qualifications. Qualifications for grade II health officers of all towns, villages, consolidated health districts and cities having less than 50,000 population remain unchanged. According to revised requirements, deputy health officers acting temporarily as health officers during the absence or disability of the health officer must possess the qualifications of a grade I-B health officer; part time, those of a grade II health officer. Amendments to the code followed a study by a special committee appointed by the public health council.

New York City

Institute of Oral Pathology.—Dr. Lloyd F. Carver, New York City, will read a paper entitled "Lymphomas and Leukemias and Their Oral Manifestations" at the monthly conference of the New York Institute of Clinical Oral Pathology at the New York Academy of Medicine, January 27, 9 p. m.

Academy Centennial.—In his inaugural address before the New York Academy of Medicine January 2, Dr. George Baehr, president, announced the centenary celebration of the academy which is to be inaugurated with a dinner at the Waldorf-Astoria Hotel March 6. Dr. John A. Ryle, formerly regius professor of physic, University of Cambridge, England, and now head of the Institute of Social Medicine, Oxford, will be the speaker.

Dr. Jarcho Honored.—Dr. Julius Jarcho, obstetrician and gynecologist, was recently honored on his retirement as president of the medical board of Sydenham Hospital at a dinner at which the hospital medical library was formally named the Dr. Julius Jarcho Library. Dr. Jarcho has served as president of the medical board during the last ten years of the forty that he has been associated with the hospital. He graduated from Columbia University College of Physicians and Surgeons in 1904.

Lectures on Venereal Diseases.—A series of free lectures for practicing physicians on diagnosis and treatment of venereal diseases have been planned by the department of health bureau of social hygiene. Meetings are held at the health department building every Saturday morning at 10:30 and will continue through April 26. Experts in special fields of venereal disease control are participating in seminars. On January 25 Dr. Leslie P. Barker, assistant professor of dermatology and syphilology, Columbia University College of Physicians and Surgeons, will discuss "Primary and Secondary Syphilis: Cutaneous Aspects and Differential Diagnosis and Treatment."

SOUTH CAROLINA

Personal.—Dr. John F. Busch, Columbia, was recently appointed assistant chief of the tuberculosis division of the department of medicine and surgery for the Veterans Administration in five Southeastern states. For the past two years Dr. Busch has been medical director of the South Carolina Tuberculosis Association.

Portrait of Dr. Boyd.—Friends and patients of Dr. William A. Boyd, Columbia, recently presented a portrait of Dr. Boyd to Columbia Hospital. The presentation address was given by Dr. Bruce Gill, emeritus professor of orthopedic surgery, University of Pennsylvania. The meeting was attended by physicians and friends of Dr. Boyd from various parts of the country.

County Society Honors Veterans.—The Greenville County Medical Society held a banquet December 2 to honor forty-four returned veterans and one member, John Dendy McBrearty, who gave his life in the service. Each veteran was given a framed scroll attesting appreciation of his efforts in World War II. A bronze plaque was unveiled to the memory of Dr. McBrearty.

TENNESSEE

Society Elections.—Dr. John C. Burch, Nashville, Tenn., gynecologist, has been elected president of the Nashville Academy of Medicine and Davidson County Medical Society, succeeding Dr. George Carpenter, Vanderbilt University.—Dr. W. J. Johnson, Pulaski, Tenn., was named president of the Middle Tennessee Medical Association at its semiannual meeting. Dr. Clarence S. Thomas, Nashville, was chosen vice president and Dr. Carl N. Gessler, Nashville, secretary-treasurer.

WEST VIRGINIA

Practical Nurse Symposium.—Sponsored by the state medical society, state nurses association and the state hospital association, a symposium on the training and service of practical nurses was held Dec. 10, 1946 at Charleston. A resolution was adopted recommending that a survey be made early in 1947 to ascertain the number of women between the ages of 18 and 50 who might be interested in a one year course in practical nursing and that such a course be developed as rapidly as interest warrants. In another resolution it was suggested that the proper officials inaugurate a refresher course without delay for practical nurses who can show evidence that they have satisfactorily worked as practical nurses within the state for the past year. Addresses were delivered by W. T. Sanger, Ph.D., Richmond, Va., president of the Medical College of Virginia; Miss Cecile Covell, R.N., nursing director Neurological Center, Presbyterian Center, New York City; Miss

Nettie Yowell, state supervisor, vocational training for women, state department of education, and Miss Hilda Torrop, R.N., president of the National Association of Practical Nurses. Miss Martha Wooddell, R.N., Clarksburg, presided at the meeting.

GENERAL

Death of Miss Beard.—Miss Mary Beard, Westport, Conn., former director of the American Red Cross Nursing Service and founder of the National Organization of Public Health Nursing, died Dec. 5, 1946 at the age of 70. Miss Beard served the Red Cross during both world wars. She wrote the book "The Nurse in Public Health." Miss Beard resigned her post in the Red Cross Nursing Service in August 1944.

American Board Examination.—The next examination of the American Board of Phychiatry and Neurology for certification in neurology and psychiatry has been tentatively set for May 15-17 in Philadelphia. Applications should be in the hands of the secretary, Dr. F. J. Braceland, 102-110 Second Avenue S.W., Rochester, Minn., ninety days before the examination is scheduled. The last possible date for filing is March 1.

Smallpox.—*Public Health Reports* for Dec. 27, 1946 summarizes the reports of smallpox cases received from various countries through January-September of that year. It is interesting in connection with the current comment concerning smallpox in this issue of THE JOURNAL that some cases of smallpox were reported from at least eighty-nine countries. The number of cases reported during that period varied from 1 each in some countries to 57,378 cases in India.

Facts About Nursing.—The Nursing Information Bureau of the American Nurses Association has prepared a booklet called "Facts About Nursing, 1946," which is a complete handbook of statistics covering every possible phase of activity in the nursing profession. Here are the data concerning the size of the profession, distribution of nurses, institutions for the education of nurses, the various fields of specialization and opportunities for employment and advancement. The pamphlet is available from the Nursing Information Bureau at 1790 Broadway, New York 19, at the price of 35 cents.

American Association for the Advancement of Science.—Twenty-six papers in a symposium on "The Rickettsial Diseases of Man" were presented before the medical sciences section of the American Association for the Advancement of Science, which met in Boston Dec. 26, 1946. Some of the other papers were on epidemic typhus, Q fever and tsutsugamushi disease. Charles F. Kettering, D.Sc., director of the research laboratories, General Motors Corporation, delivered the retiring president's address on the future of science. President James Bryant Conant of Harvard University is the incoming president of the association.

Narcotic Violations.—The Bureau of Narcotics reports that Dr. W. D. Maag, Jeffersonville, Ohio, pleaded guilty at Columbus, Ohio, to violation of the federal narcotic law and on Nov. 25, 1946 was sentenced to a term of three years.——Dr. Harry Alonzo K. Hill, Laverne, Okla., pleaded guilty to violation of section 2554(a) of the Internal Revenue Code in the U. S. District Court at Oklahoma City, Okla., and on Nov. 20, 1946 his sentence of five years was suspended and he was placed on probation for a like period. He was also fined the sum of $500, according to an announcement from the Bureau of Narcotics, Washington, D. C.

Essay Contest.—The seventh annual essay contest of the Mississippi Valley Medical Society offers for 1947 a cash prize of $100, a gold medal and a certificate of award for the best unpublished essay on a subject of medical interest and practical value to the general practitioner of medicine. Contestants must be members of the American Medical Association who are residents of the United States. The winner will present his contribution before the Mississippi Medical Society in October. Manuscripts must be received not later than May 1. Further details may be secured from Dr. Harold Swanberg, secretary, Mississippi Valley Medical Society, 209-224 W. C. U. Building, Quincy, Ill.

Seeing Eye Dog Hoax.—Unfounded reports continue to circulate that a blind person can obtain a Seeing Eye dog by collecting quantities of tinfoil, empty paper match folders, cigaret packages or similar articles, warns Edward L. Greene, general manager of the National Better Business Bureau. These stupid rumors, Mr. Greene states, still gather in new victims despite unceasing work to stamp out the hoax by the press, the Better Business Bureaus and the commercial companies innocently involved; and scores of blind persons have saved thousands of useless articles, some with the help of their entire community, only to find that their work was in vain. The Seeing Eye of Morristown, N. J., has repeatedly stated that blind persons desiring a dog should write directly to the organization for particulars.

Society for Study of Sterility.—The first annual conference for the Western Branch of the American Society for the Study of Sterility will be held in Los Angeles February 7-8 to discuss advances in the management of the barren marriage, with particular reference to clinical applications. Topics to be discussed include the social aspects of infertility, role of the hypothalamus, nutritional deficiencies, management of habitual and threatened abortion, physiology of spermatogenesis, the control of ovarian activity, hyalouronidase, semen evaluation, testicular biopsy and hormonal assays. Among the speakers are Drs. Benjamin B. Weinstein, Tulane University School of Medicine, and Carlos D. Guerrero, Mexico City. Further information may be secured from Dr. A. R. Abarbanel, Secretary Program Committee, 441 South Beverly Drive, Beverly Hills, Calif.

Professor Whitby Returns to England.—Sir Lionel Whitby, regius professor of physic, University of Cambridge Department of Medicine and honorary consulting hematologist to the Royal Army Medical Corps, returned to England November 29, having been in this country since October 21. During his stay in the United States he delivered the Hunter Memorial Lecture at the Peter Bent Brigham Hospital, Boston; the Eastman Memorial Lecture at the University of Rochester School of Medicine and Dentistry, Rochester, N. Y., and the A. C. Helmholz Lecture at the University of Wisconsin Medical School, Madison. He was also guest lecturer at Western Reserve University School of Medicine, Cleveland; Ohio State University College of Medicine, Columbus; the University of Michigan, Ann Arbor; the Chicago Institute of Medicine, and the State University of Iowa College of Medicine, Iowa City. Sir Lionel, who is said to have been the first physician to apply sulfapyridine to clinical practice, is well known as the co-author of a textbook on hematology.

Nobel Prize Winners in 1946.—At a ceremony in Stockholm, Dec. 10, 1946, King Gustav of Sweden awarded the Nobel Prize in Medicine and Physiology to Herman Joseph Muller, Ph.D., professor of zoology at Indiana University, Bloomington, Ind., and formerly professor of biology at Amherst College, Amherst, Mass., for his research in genetics. The award in chemistry was shared by three men, one half going to James Batcheller Sumner, Ph.D., professor of chemistry at Cornell University, Ithaca, N. Y., for his research on enzymes; the other half was awarded jointly to John Howard Northrop, Ph.D., and Wendell M. Stanley, Ph.D., of the Rockefeller Institute, Princeton, N. J., for their research on virus proteins. The Nobel prize in physics was awarded to Percy Williams Bridgman, Ph.D., formerly professor of physics, Harvard University, Cambridge, Mass., and since 1926 professor of mathematics and natural philosophy, for his research on atmospheric pressure. About 500 persons, including the entire royal family, witnessed the ceremony in the Concert House and attended the prize dinner in the Town Hall. Each of the Nobel prizes was worth $34,000.

Special Society Elections.—At the recent annual convention of the American Academy of Dermatology and Syphilology, Dr. Edward A. Oliver, Chicago, professor of dermatology at Northwestern University, was elected president.——Dr. E. Harold Hinman was chosen president-elect of the National Malaria Society at its twenty-ninth annual meeting in Miami, Fla., Nov. 4 to 7, and Dr. Mark D. Hollis was installed as president.——Dr. Willard O. Thompson, Chicago, was chosen president-elect of the Mississippi Valley Medical Society during its eleventh annual meeting recently, and Dr. Walter A. Sternberg, Mount Pleasant, Iowa, was inducted into the presidency. ——The newly elected officers of the Central Association of Obstetricians and Gynecologists are as follows: Drs. Earl C. Sage, Omaha, president; William F. Mengert, Dallas, Texas, president-elect; George A. Kamperman, Detroit, vice president; John I. Brewer, Chicago, secretary-treasurer, and Harold L. Gainey, Kansas City, Mo., assistant secretary-treasurer.——At the fifty-eighth annual session of the Southern Surgical Association in Hot Springs, Va., Dec. 10-12, 1946 Dr. Frank S. Johns, Johnston-Willis Hospital, Richmond, Va., was elected president. Vice presidents named were Dr. Charles Reid Edwards, Baltimore, and Dr. Frank C. Wilson, Birmingham, Ala.——Dr. Irvin Abell, clinical professor of surgery, University of Louisville School of Medicine for over forty years, was

inaugurated president of the American College of Surgeons at the recent meeting in Cleveland. Dr. Abell is a past president of the American Medical Association, the Southern Medical Association and the Southern Surgical Association.

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Frederick York Durrance ✦ Houston, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1925; specialist certified by the American Board of Radiology, Inc.; member of the Radiological Society of North America, Inc., and the American College of Radiology; associate professor of radiology at the Baylor University College of Medicine; chief of the radiologic department of the Hermann Hospital; died Oct. 29, 1946, aged 53, of coronary thrombosis.

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Robert Elisha Downing, Lexington, Ky.; Emory University School of Medicine, Atlanta, Ga., 1930; specialist certified by the American Board of Radiology; member of the American Medical Association, Radiological Society of North America and the American College of Radiology; on the staff of the Good Samaritan Hospital of Lexington; served during World War II; died in Brewton, Ala., Oct. 5, 1946, aged 41, of coronary occlusion.

Melvin Dresbach, Philadelphia; Ohio Medical University, Columbus, 1903; served on the faculties of the Cornell University in Ithaca, N. Y., Albany (N. Y.) Medical College, Ohio State University and Starling-Ohio Medical College in Columbus; member of the American Physiological Society and of the Society for Experimental Biology and Medicine; died Oct. 15, 1946, aged 72, of coronary occlusion.

Frederick York Durrance ✦ Houston, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1925; specialist certified by the American Board of Radiology, Inc.; member of the Radiological Society of North America, Inc., and the American College of Radiology; associate professor of radiology at the Baylor University College of Medicine; chief of the radiologic department of the Hermann Hospital; died Oct. 29, 1946, aged 53, of coronary thrombosis.

Henry Theodore Foshager ✦ Clara City, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1909; died in Stoneham township Oct. 19, 1946, aged 65, of injuries received in an automobile accident.

John Paulett Haller, Salem, Va.; Medical College of Virginia, Richmond, 1882; member of the American Medical Association; died Oct. 24, 1946, aged 85, of Parkinson's disease.

Byrt Boone Hutton, Harrisburg, Ill.; Barnes Medical College, St. Louis, 1908; member of the American Medical Association; at one time president of the Saline County Medical Society; on the staff of the Lightner Hospital; died in the Lutheran Hospital, St. Louis, Oct. 22, 1946, aged 62, of atelectasis of the right lower lobe, diverticulum of the sigmoid and cirrhosis of the liver.

John Paul Jones, Mitchell, S. D.; Northwestern University Medical School, Chicago, 1939; member of the American Medical Association; began active duty as a captain in the medical corps, Army of the United States, in Feb. 8, 1941; spent three years in the European theater; discharged as a major Sept. 9, 1945; resumed practice in November 1945; on the staff of St. Joseph Hospital and Methodist State Hospital, where he died Oct. 30, 1946, aged 36, of pneumonia.

John Arthur Kneller, Attica, N. Y.; University of Buffalo School of Medicine, 1912; member of the American Medical Association; served as county coroner and mayor; health officer of Bennington township; died in the Buffalo General Hospital Oct. 20, 1946, aged 57, of nephrosclerosis and hypertension.

George W. McFatrich, Chicago; Bennett Medical College, Chicago, 1891; interned at the Cook County Hospital, where he was ophthalmologist; died in the Passavant Memorial Hospital Nov. 10, 1946, aged 76, of intracranial hemorrhage.

Marion Blanche Neil, Forest City, Iowa; Northwestern University Woman's Medical School, Chicago, 1901; formerly in charge of social welfare work in Winnebago County; died Oct. 9, 1946, aged 68, of coronary artery disease.

Ivo Amazon Nelson, Tulsa, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1925; specialist certified by the American Board of Pathology, Inc.; member of the American Society of Clinical Pathologists; served as pathologist on the staff of St. John's Hospital; associated with the Nelson Pathological Laboratories, which he founded; died Oct. 21, 1946, aged 52, of myocardial failure.

Otto Charles Pinc ✦ Chicago; Rush Medical College, Chicago, 1924; interned at the Kings County Hospital in Brooklyn; resident physician at the Cook County Infirmary in Oak Forest, Ill.; on the staff of the Bethany Sanitarium and Hospital; captain, medical reserve corps, U. S. Army, not on active duty; died in the Albert Merritt Billings Hospital Nov. 9, 1946, aged 46, of hypertension and cardiovascular disease.

David Giltner Pryor, Jeffersonville, Ind.; University of Louisville (Ky.) School of Medicine, 1931; member of the American Medical Association; president of the staff of the Clark County Memorial Hospital; served as president of the Rotary Club; died Oct. 27, 1946, aged 43, of coronary occlusion.

George W. Sargent, Seneca Castle, N. Y.; Syracuse University College of Medicine, 1879; member of the American Medical Association; served as health officer; died Oct. 1, 1946, aged 93, of arteriosclerosis.

Anton Henry Schaefer, Berkeley, Calif.; Stanford University School of Medicine, San Francisco, 1941; member of the American Medical Association; interned at the Alameda County Hospital in Oakland; served a residency at Ernest V. Cowell Memorial Hospital; died in Alta Bates Hospital Sept. 29, 1946, aged 41, of lymphosarcoma.

Cortlandt Whitehead Schepeler ✦ Brooklyn, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1915; served during World War I; on the staffs of the Mercy Hospital and the Foote Memorial Hospital, where he died Oct. 27, 1946, aged 55, of cerebral hemorrhage.

Joseph Otto Segura, Jackson, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1910; member of the American Medical Association; vice president and medical director of the Lamar Life Insurance Company; served in England during World War I; died in a hospital at Abbeville, La., Oct. 26, 1946, aged 59, of coronary occlusion.

Jeannette M. Shefferd ✦ Fall River, Mass.; John A. Creighton Medical College, Omaha, 1912; specialist certified by the American Board of Otolaryngology; member of the New England Otological and Laryngological Society; on the staff of the Union Hospital, where she died Oct. 23, 1946, aged 67, of carcinoma of the colon.

Joseph Scott Snider ✦ Kansas City, Mo.; University Medical College of Kansas City, Mo., 1900; served during World War I; an Affiliate Fellow of the American Medical Association; on the staff of St. Mary's Hospital, where he died Oct. 29, 1946, aged 70, of carcinoma of the right lung.

Charles C. Snowden, Davenport, Neb.; Jefferson Medical College of Philadelphia, 1882; member of the American Medical Association; died in Lincoln Oct. 25, 1946, aged 91, of pneumonia.

David Henry Stern, Hammond, Ind.; University of Illinois College of Medicine, Chicago, 1937; member of the American Medical Association; served during World War II; on the staff of St. Margaret Hospital, where he died June 13, 1946, aged 38, of coronary thrombosis.

Rae Latham Strong ✦ Bloomingdale, N. Y.; University of Buffalo School of Medicine, 1899; for many years health officer; on the staffs of Champlain Valley and Physicians hospitals in Plattsburg and General Hospital in Saranac Lake, where he died Oct. 18, 1946, aged 70, of arteriosclerosis.

John William Thomson ✦ Garrett, Ind.; Rush Medical College, Chicago, 1909; for many years president of the school board; past president of the De Kalb County Medical Society and of the Northeastern Indiana Academy of Medicine; served during World War I; member of the American Association of Railway Surgeons; surgeon for the Baltimore & Ohio Railroad; on the staffs of the Sacred Heart Hospital in Garrett and the McCray Memorial Hospital in Kendallville; died Oct. 17, 1946, aged 60, of uremia.

DIED WHILE IN MILITARY SERVICE

Hubert Benjamin Bradburn ✦ Lincoln, Ill.; Washington University School of Medicine, St. Louis, 1927; fellow of the American College of Surgeons; formerly city physician; served an internship and as resident physician at the Vanderbilt University Hospital in Nashville, Tenn.; began active duty as a captain in the medical corps, Army of the United States, on July 17, 1942; promoted to major; died in the Walter Reed General Hospital, Washington, D. C., Sept. 4, 1946, aged 45, of mesenteric thrombosis.

Harold Edward Hanley, Richmond Hill, N. Y.; New York University College of Medicine, New York, 1943; interned at the Bellevue Hospital in New York; began active duty as a first lieutenant in the medical corps, Army of the United States, on Oct. 15, 1944; following his assignment in Hawaii was stationed in Japan, where he was attached to the 98th Division and where he died May 23, 1946, aged 27, of a skull fracture received in an accident.

Isaac Newton LaVictoire, Pigeon, Mich.; Yale University School of Medicine, New Haven, Conn., 1928; member of the American Medical Association; interned at the Conemaugh Valley Memorial Hospital in Johnstown, Pa.; served a residency at the Kalamazoo State Hospital in Kalamazoo; at one time affiliated with the State Prison of Southern Michigan in Jackson and the Michigan Reformatory in Ionia; commissioned a lieutenant (jg) in the medical corps of the U. S. Naval Reserve in 1933; began active duty in February 1941; sent to the Philippines and was stationed at Cavite naval base near Manila when the Japanese struck; fought with the navy until the fall of Cavite; moved to Manila, where he fell prisoner of the Japs; imprisoned for three years at the Cabanatuan prison camp; shortly after the invasion of the Philippines by American forces the prison camp was liberated by American rangers and he was one of the 483 American personnel liberated; promoted through the grades to captain; died March 2, 1946, aged 43, of coronary thrombosis and general debility incurred while a prisoner of war of the Japanese.

Maurice James McElligott, Lynn, Mass.; Rush Medical College, Chicago, 1937; member of the American Medical Association and the Illinois State Medical Society; interned at the Boston City Hospital in Boston, where he served a residency; served a residency at the Westfield State Sanatorium in Westfield; captain in the medical corps, Army of the United States; died in Denver April 25, 1945, aged 42, of coronary occlusion.

Frank W. Wilson ✦ Colonel, M. C., U. S. Army, Swannanoa, N. C.; University of Maryland School of Medicine, Baltimore, 1914; Army Medical School in 1916; Medical Field Service School Advanced Course, Carlisle Barracks, in 1934; born in Greenville, N. C., April 29, 1888; fellow of the American College of Physicians; member of the Medical Association of Georgia; specialist certified by the American Board of Internal Medicine; given a reserve commission in the medical service of the army in August 1915 and appointed to the medical corps in 1916; served on the Mexican border, followed by overseas duty in World War I; had three tours of duty at Walter Reed Hospital in Washington and a long period of service at Fort Benning, Ga.; placed in charge of the Station Hospital at Camp Shelby, Miss., in 1940; assigned to command the Moore General Hospital in 1942 when it was established and where he died April 20, 1946, aged 58, of coronary thrombosis.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Dec. 30, 1946.

Body Temperature as Guide to Determining the Time of Death

Dr. C. Keith Simpson, medicolegal pathologist, who has done remarkable work in the identification of the mutilated and buried remains of a murdered woman, recently gave attention to deciding how long a person has been dead (*Science Progress,* October 1946, p. 713). He holds that the most reliable guide is the steady fall of temperature which takes place for twenty-four hours after death. Under average conditions he finds that about 2.5 degrees F. is lost hourly for the first six hours and from 1.5 to 2 degrees F. hourly for the next six hours. Calculations based on these figures may be upset by extremes of temperature, the amount of clothing worn, ventilation and environment. Thus a body in a river will reach the temperature of the surrounding atmosphere much more quickly than one on dry land. If parasites such as fleas and lice are present, the entomologist may help by finding out whether they are still alive and, if so, how long it takes to revive them. Adipocere may hinder rather than help, for hydrogenation of body fat is variable. With warmth it may take place in three or four weeks or it may be delayed beyond the four or five months which is the average in England. The onset of rigor mortis or of postmortem lividity is of little use in deciding the time of death. Simpson concludes that in estimating the time of death the most reliance is to be placed on the body temperature. It is never too late, he says, to measure this. Though the body is cold it may still register a few degrees above its surroundings. As an example he cites a murder in which the body temperature was still 7 degrees F. above the temperature of the air, although it had lain eighteen hours in the snow. This made it possible to fix the time of death within an hour.

Government Plan for Taking Over the Voluntary Hospitals

The voluntary hospitals are so called because they were founded and until recent years were entirely supported by the voluntary subscriptions of the charitable. They comprise the great hospitals which are medical schools. Following closely the passage of the National Health Service Act the Ministry of Health has produced an elaborate plan for taking over all the hospitals, though it does not propose to interfere with the autonomy of the medical schools. For purposes of administration the whole country has been mapped into areas, each with a university medical center as a focal point—Manchester, Leeds, Birmingham, Sheffield, Liverpool, Bristol, Newcastle, Cardiff, Oxford and Cambridge. London has four areas, northwest, northeast, southeast and southwest, each extending into the adjacent country. For all these areas regional hospital boards are to be appointed to administer the hospital and specialist services. For the benefit of any observations which may be made the Ministry of Health has issued a circular to the local bodies and organizations concerned. The size and extent of the areas will be determined by their purpose, which is to provide an area adapted rather for the planning, coordination and provision of hospital and specialist services rather than for the control and management of hospitals. The latter task will be the function of hospital management committees. It follows that the areas must be comparatively large in population. The boundaries of the areas will not prevent patients from freely passing from one area to another. Whenever possible the boundaries of the areas should coincide with those of local health authorities, but other important factors, such as association of services with medical schools or grouping of related hospitals with the same regional board, make it necessary to cross such boundaries.

Anglo-French Medical Cooperation in West Africa

At an Anglo-French medical conference held at Accra, Gold Coast, West Africa, a system of cooperation in many aspects of public health and medical work in the West African territories was agreed on. Pathologic laboratories in the area will be used according to geographic convenience rather than international boundaries. It is hoped to organize during the coming year experiments in joint campaigns in frontier areas where the ravages of sleeping sickness, smallpox or yellow fever occur on both sides of the border. The conference had its origin in arrangements for closer Anglo-French cooperation in colonial matters, but experts who attended from the Belgian Congo and from Portugese Guinea and Liberia expressed agreement with the principles underlying the recommendations and their desire to develop similar cooperation.

BUENOS AIRES

(From Our Regular Correspondent)

Nov. 5, 1946.

Discussion on Experimental Diabetes

At a recent meeting of the Sociedad Argentina de Biologia, Drs. B. A. Houssay, R. F. Brignone, A. F. Cardeza and J. G. Sara, of Buenos Aires, reported experiments on dogs which had transient diabetes after the injection of alloxan and which developed permanent diabetes after prolonged treatment with thyroid. This form of metathyroid diabetes from alloxan is a pancreatic diabetes due to lesion on the beta cells of the islands of Langerhans (degranulation and strong diminution in number). The administration of thyroid does not produce diabetes unless the resistance of the pancreas has been diminished and the condition of the pancreatic beta cells has been changed.

Dr. C. Martinez discussed the influence of hyperthyroidism on alloxan and pancreatic diabetes in white rats: (*a*) thyroid administered for twenty consecutive days increases sensibility to alloxan, whereas if it is given for sixty consecutive days it gives the animals a supernormal resistance; (*b*) thyroid treatment of rats after ample pancreatectomy (removal of 95 per cent of the pancreas) causes the appearance of diabetes in the first two weeks of treatment. After this period of time diabetes gradually disappears even if the administration of thyroid is continued; (*c*) thyroid treatment of rats with ample pancreatectomy in the early period of diabetes causes total disappearance of diabetes, and (*d*) the favorable effect of thyroid seems to be due to stimulation of the pancreatic islands and to hyperplasia.

Drs. S. Gitter and A. F. Cardeza discussed the diabetogenic effect of substances with chemical resemblance to alloxan, namely, alloxantin, methylalloxan and dialuric, barbituric and violuric acids. Two different histologic types from the diabetogenic effect are observed in the islands of Langerhans: (*a*) coagulation necrosis of the beta cells (from alloxan, alloxantin and dialuric acid) and (*b*) degeneration of the beta cells without coagulation necrosis (from either barbituric or violuric acids).

Drs. B. A. Houssay and P. Mazzocco discussed the effects of either diethylstilbestrol or alloxan on glycemia and glycogen in rats. Administration of sugar after fifteen hours of fasting to rats either normal or with alloxan diabetes, causes a more acute hyperglycemia and a smaller amount of glycogen in the liver and muscles of the latter than in those of the former. Administration of sugar after fifteen hours of fasting to rats, either normal or with alloxan diabetes which had diethylstilbestrol treatment, caused an increase of glycemia, moderate in normal rats and acute in rats with alloxan diabetes. The increase of the hepatic and muscular glycogen was moderate in normal rats and acute in rats with alloxan diabetes.

Dr. Carlos Martinez discussed age in relation to diabetes in rats. Subtotal pancreatectomy (95 per cent) in male rats aged 10 days caused noncomplicated benign diabetes in a small percentage of the animals. In animals aged 547 days, or more, it caused in almost all the early appearance of diabetes of acute course and complicated by acute infections and the early appearance of cataracts. Progressive loss of body weight was acute and mortality high (75 per cent) in this group. In rats aged 60 to 70 days, diabetes occurred in all the animals in the lot. The mortality was 25 per cent in this group. The results of the experiments show that in young animals the pancreas has a better opportunity for regeneration after pancreatectomy. Because of the size of the pancreas at this age, it is probable that the removed portion of the structure is smaller than one believes during performance of experimental pancreatectomy. The number of island cells is greater in young rats than in adult rats.

Drs. E. Moisset de Espanés, B. Weksler and E. Ortega, of Cordoba, reported results of experiments of studies on the toxicity of alpha-fagarine. The following results were encountered: One hundred male rats (Wistar strain) had intraperitoneal injections of alpha-fagarine solutions. The values of the lethal dose (50 per cent) varied from 90 to 117.1 mg. for each kilogram of body weight, in accordance with different methods used for its determination. The greatest tolerated dose is 74 mg. for each kilogram of body weight. The lethal dose (100 per cent) is 196 mg. for each kilogram of body weight. The lethal dose (50 per cent) for dibencyl-methyl-amine in rats, by intraperitoneal route, is 656 mg. for each kilogram of body weight. Consequently alpha-fagarine is 7.17 ± 1.44 times more toxic than dibencyl-methyl-amine. Determinations of the toxicity of alpha-fagarine were also carried out on rabbits. Ten lots of rabbits each had intravenous injections of alpha-fagarine solution in doses which varied from 2 to 4 per cent. The average lethal dose (LD 50) varied between 14 and 20 mg. for each kilogram of body weight, according to the different methods used for the determination. The greater tolerated dose (LD 0) was about 4 mg. for each kilogram of body weight and the 100 per cent lethal dose (LD 100) was 30 mg. for each kilogram of body weight. The response to the effect of alpha-fagarine was more uniform in rats than in rabbits.

Retirement of University Professors

The statute of the National University of Buenos Aires makes 65 the retirement age of professors, unless the person wishes to retire five years earlier. Through a decree, this regulation was modified for all the universities in the country. Professors retire in accordance with the law for civilians working in public administration, by which employees retire at age 55 and after thirty years of work. The new regulation has been applied to the University of Buenos Aires. The professors immediately eligible for retirement according to the new regulation included Drs. B. A. Houssay, Alejandro Ceballos, José María Jorge and Juan A. Gabastou, who were declared dismissed through retirement. Drs. Eduardo Braun Menéndez and R. Foglia of the Faculty of Medical Sciences of Buenos Aires, Oscar Oria and E. Moisset de Espanés of the Faculty of Cordoba and J. T. Lewis of the Faculty of Rosario resigned because of the dismissal of Dr. Houssay.

Dr. Houssay, who is 59 years old, received this news just as he was leaving Argentina to attend special ceremonies in Canada and the United States in celebration of the 25th anniversary of the discovery of insulin. The University of Toronto gave Dr. Houssay the 1945 "Charles Micle" prize for his work in medicine. He delivered important lectures at the University of Toronto, the National Academy of Sciences in Washington, the American Philosophical Society of Philadelphia and other universities. He was recently appointed Professor honoris causa of the Universities of Brazil, Lyon (France) and Montreal.

JAPAN

(From a Special Correspondent)

Tokyo, Nov. 1, 1946.

Reform of Medical Education in Japan

An important innovation in Japanese medicine will be the establishment of a modern internship system throughout the country. Under the guidance of Major S. E. Molten, chief laboratory consultant for the public health and welfare section of general headquarters, an archaic system wherein postgraduate students often remained behind in their university hospitals to work for higher degrees will be abandoned. In prewar Japan these students seldom had an opportunity to assume actual responsibility for patients. An average clinic in these university hospitals could have two interns assigned to each patient. This concentration of young doctors in a few medical centers will cease to be a general characteristic of Japanese medicine as a general reform program of the Education and Health ministries gets under way. It is intended that the number of beds in the metropolitan hospitals which are available for internship assignment will be carefully limited. Present plans, calling for the enforcement of a quota of 10 to 25 patients to the care of one intern, will cause a migration of young interns to smaller cities and prefectural health centers in Japan. It is hoped by allied officials that such a move will tend to liberate Japanese medicine and medical education from their tendency toward citadelism and the throttling effect of academically isolated cliques among members of the profession. Assignment of interns from more than one school to a particular hospital is intended to produce an overlapping of school influences. This should result in an active exchange of specialized knowledge and constructive criticism of personal technics. Example and competition have always proved a major factor in elevation of medical standards.

It would not be incorrect to epitomize this sweeping reform in the intersystem of Japan as the assumption of much greater responsibility on the part of young Nipponese doctors. As part of the general medical reform they will now work as doctors and not students during the period of internship. Older and more experienced doctors will be expected to engender in their disciples the true meaning of responsibility and trust. American public health officers hope that this change will also benefit the experienced doctors and surgeons, for in their meeting and working with young interns who are full of enthusiasm and theory they will be exposed to what is new in turn for teaching what is old but yet true. Major Molton has signified this plan as "the old idea of apprenticeship brought up to date for the benefit of medicine in Japan."

Living Quarters for Interns

Still unsolved by most hospitals in occupied Japan is the problem of adequate living facilities for interns. Since few of the hospitals in this country are operated on a nonprofit basis it is difficult to discuss with them the value of an internship in terms of financial outlay. No immediate remedy is expected by occupation officials. It is hoped that hospitals will come to realize the true value of good interns. The result of this change in attitude should be a healthy competition for young doctors together with concurrent improvement in living quarters and intern pay. Some progress in this matter can already be noted where the "medical center" idea is taking hold in a few large cities. Another change in the curriculum of study-practice followed by Japanese interns since the war, and one employed nowhere else in the world (to my knowledge) is the provision for one month of work by each intern in an approved health center at the prefectural level. Taking the intern out of the Japanese metropolis and sending him to such a local health unit means that he is doing actual field work in the public health sphere of activities. This plan should result in many more doctors who are conscious of problems of a public health nature.

Correspondence

TREATMENT OF VARICOSE VEINS

To the Editor:—Dr. Gerald H. Pratt's article on the Treatment of Varicose Veins, in THE JOURNAL, Nov. 23, 1946, suggesting the use of interval suspension of the distal stem of the resected "blowouts" in varicose vein surgery, proves further to me that the work of Dr. R. Stanton Sherman of San Francisco is the closest approach to complete success. If the workers in this field will refer back to his articles, starting with *California and Western Medicine* in September 1942, through the later ones in the *Annals of Surgery* in November 1944, they will find the anatomic basis for his extensive operative procedure of bilateral high saphenous vein ligation, perforator interruption and stripping, with short saphenous ligation and perforator interruption, as well, in many cases where it is indicated.

The anatomic pattern of the venous system of the lower extremity is easily visualized in cross section roughly as a wagon wheel. The hub represents the deep venous circulation, whereas the rim represents the superficial or saphenous system. The spokes represent the leaking incompetent perforators. Through this system the venous blood circulates, and in cases of varicosis with leaking valves in the saphenous and communicating or perforator veins the greater pressured deep venous blood runs backward to fill the outer system at the many levels of incompetent perforators. The latter, mainly, are the saphenofemoral junction, mid-Hunter canal area and the geniculate and short saphenous veins about the knee and various sites in the leg. The latter have been described in great part by Dr. Linton.

To eliminate "blowouts" per se is not eliminating leaking perforators, as the location of the former does not necessarily signify the location of the entrance of the perforators into the deep system except in the leg at certain sites. The perforators of the thigh and knee run obliquely upward and inward, and their entrance into the deep system is therefore higher than the location of a "blowout," and they must be ligated close to the deep femoral vein, not in the superficial tissues. A "blowout" may also not be at the site of any leaking perforator.

My own operative experience coincides with that of Dr. Pratt in that approximately one fourth to one third of all my cases are ones previously treated with high saphenous vein ligation alone or with interval saphenous vein or "blowout" ligation in addition. There is a great deal more accurate knowledge necessary in regard to the sites of the perforators of the thigh and leg. Sherman has added greatly to our knowledge of these, particularly of the thigh and knee regions, by his contributions. The sites of leaking perforators of the anterior, mesial and posterior leg are also quite well established. The mesial lower leg perforators, 18-20 cm. above the sole of the mesial border of the foot, mentioned by Sherman, are more or less constant offenders. Their presence cannot always be definitely determined before exploration. When the perforator locations are definitely known, we shall then achieve greater success in their elimination and we shall not have to depend on tests for their presence. Leakage from them is present in practically all cases. All tests, at best, are only partially helpful.

Referring back to the similarity of the venous system to a wagon wheel, real success will come only when all spokes of the wheel are interrupted at all levels at which they occur, as far back toward the hub as we can possibly go.

ROBERT A. OSTROFF, M.D., Beverly Hills, Calif.

ENURESIS

To the Editor:—In the November 30 issue of THE JOURNAL a communication from Dr. Edwin E. Ziegler, appearing under Correspondence, recommends the "start and stop" method of treatment for enuresis. I was impressed with this regimen while working in the Behaviour Clinic of the late Dr. Ira S. Wile in 1924 and subsequently used it in my own clinic at the University of Nebraska College of Medicine.

There seems to be one insurmountable difficulty with the procedure. It is true that many enuretic persons, if not all, suffer from a loss of confidence in their ability to control their urinary bladders. The "start-stop" method, in some cases at least, convinces these youngsters that they do have voluntary control if they choose to exercise such control. There was not a single child in my clinic who ever missed an opportunity to express pride and happiness in his achievement, and even bad enuretic patients went from one to several weeks without "accident."

To my chagrin, however, these boys and girls soon began to return in increasing numbers with downcast features, each with the same story. They were so enthusiastic about the procedure that they commenced to practice it in their sleep. In the group was 1 boy aged 11 who was suffering from diurnal enuresis and who was so preoccupied with resentment toward one of his teachers that he began unconsciously to "start and stop" while daydreaming in the classroom. He "guessed" forlornly that he had more confidence in starting than in stopping. His enuresis cleared up shortly after he had been transferred from parochial to public school.

The current belief among pediatricians that enuresis as a bad habit has greater social than medical implications is, in my opinion, logical indeed.

HERMAN M. JAHR, M.D., Omaha.

SUCROSE TOLERANCE TESTS

To the Editor:—In regard to the item on "Sucrose Tolerance Tests," published in Queries and Minor Notes in THE JOURNAL, Sept. 14, 1946, page 116, in which it is stated that sucrose tests have not been done in large enough numbers for statistically significant normals to be established, we think it might be of some help to your correspondent to offer you the results of our investigations on the effects of the ingestion of 100 Gm. of sucrose on the blood sugar and levulose levels in 100 normal persons. These results were communicated to the Physiological Society of Great Britain in 1942. As wartime conditions prevented publication of the complete details, we attach a summary of our results.

Average Normal Values and Standard Deviations After Ingestion of 100 Gm. of Sucrose

Fifty Male and Fifty Female Controls, in Milligrams per Hundred Cubic Centimeters

	Male		Female	
	Blood Sugar	Blood Levulose	Blood Sugar	Blood Levulose
Fasting	83±10	2.6±0.58	78±10	2.2 ±0.3
¾ hr. after sucrose..	123±24	6.6±1.5	110±19	5.5 ±1.2
1½ hr. after sucrose..	89±17	6.7±1.4	84±18	6.2 ±1.2
2 hr. after sucrose....	78±15	5.3±1.0	77±15	5.25±1.1
2½ hr. after sucrose..	77±12	3.9±1.0	73±13	3.9 ±1.0

We have since shown that the sucrose test is a reliable test of liver damage (*Brit. M. J.* **1**:212 [Feb. 12] 1945. Some Early Effects of Exposure to Trinitrotoluene, *Brit. J. Indust. Med.* **2**:74, 1945).

J. R. P. O'BRIEN,
G. HIGGINS,
Department of Biochemistry,
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ENDOCRINE THERAPY IN MALE STERILITY OF NONENDOCRINE ORIGIN VALUELESS

To the Editor:—Despite the fact that reputable clinicians are now in accord that endocrine treatment of male sterility of nonendocrine origin is futile, such therapy is still widely in vogue. Apparently, even a number of honest physicians are still "trying out" glandular injections for azoospermia and severe oligozoospermia with no endocrine basis whatever. Much of the blame for continuing this therapy undoubtedly falls on the shoulders of some pharmaceutical houses, still advertising treatment of male sterility by hormone injections, etc., based on so-called "clinical reports." On close scrutiny of these "clinical reports" one finds that they consist of either old outdated articles or reports from some physicians whose papers give mute evidence of unscientifically controlled experiments, wild imagination, wishful thinking and probably even microscopic mirages.

In an attempt to reach the masses of physicians to forestall further useless therapy, a few brief notes from a paper to be published in detail elsewhere follow.

On my return from service in 1946, in a follow-up study, I contacted many of my former childless couples and asked to see them. In the years that had elapsed, some had had babies and others had not. Most interesting were the cases of 36 husbands who had received endocrine treatment in my absence. Previouly, I had given each of these men little or no hope for future procreativity. Each had been personally diagnosed as sterile, or so extremely oligozoospermic as to be practically sterile. For example, in this drastic oligospermic class the general status of the semen was such that the observer had to search under the high power for a few spermatozoa—living, dead or otherwise. In none of these specimens had there been a count of more than 5 million spermatozoa per cubic centimeter.

In the follow-up, attempts were carefully made to obtain information regarding the type, amount and duration of therapy. It is significant that a number of the physicians contacted, reported to me that they had treated the particular patient in question only as a result of urging from the patient himself or the patient's wife. It was found that all types, doses and combinations of endocrine medicaments had been used, including large doses of estrogens and androgens (now known to be sperm-inhibiting). Treatments lasted on the average about three months.

In the process of rechecking, each of the 36 passed a properly collected specimen. I, personally, examined each semen. The findings were as anticipated. Nine men who had been completely azoospermic were still azoospermic. Twenty-five with severe depletion of spermatozoa were practically unchanged—in not one of these men was any appreciable evidence of improvement found. Two men, in whose semen I had found in 1943 an occasional sperm cell, now showed complete azoospermia following an intensive course of testosterone treatment.

It cannot be too strongly emphasized that the cause of the vast majority of cases of infertility in the male has not yet been determined. Most of them in private practice are nonobstructive, nonendocrine and without history of scrotal swelling following mumps. Lowered male fertility, aside from those instances in which a definite cause can be elicited, may simply be a congenital failing. Certainly, endocrine therapy where there is no evidence of endocrine deficiency is foolhardy and at times even deleterious.

May I suggest that restraint be practiced in the treatment of male infertility until some form of proved therapy, supported by reputable scientists, is made available. In this connection, based on the original investigations of McClean and Rowlands (England) with the enzyme hyaluronidase, Kurzrok in this country has reported preliminary experiments using this substance in male infertility which bear watching.

Abner I. Weisman, M.D., New York.

APPARENT SENSITIVITY TO AMIGEN

To the Editor:—I am writing you concerning the clinical report by Harris, Gordon, Gray and Barton on "Apparent Sensitivity to Amigen," which appeared in The Journal, November 30, page 785.

It seems to me not only that this report lacks scientific objectiveness but that the authors have certainly not established any proof of sensitivity to Amigen. No evidence was adduced that this reaction was not based on the administration of pyrogen or contaminated solution. There was no culture of the Amigen solution reported or any other study of the material that they gave. The conclusion certainly is not warranted by the evidence which the authors present that the reaction was due to a foreign protein inherent in the manufactured solution. The descriptive literature of the product states that every batch of this material is tested on guinea pigs for its anaphylactogenicity and the absence of protein very carefully established. Since the authors of this report made no effort to prove that protein was present, it seems hardly justified to attribute the reaction to this cause without proof in a case so otherwise involved.

Casein hydrolysates are excellent culture mediums, and reactions to such solutions may occur as a result of contamination or the presence of pyrogens due to poorly washed equipment. The report as an instance of apparent sensitivity to Amigen seems unwarranted by the evidence submitted.

Physicians, I am sure, are deeply interested in proved instances of sensitization or other proved reactions to casein hydrolysate itself, but poorly documented papers of this type are untimely and only confuse the subject by attributing reactions of all types to sensitization without adequately investigating other causes.

H. G. Poncher, M.D., Chicago.

DEMEROL IN ITALY

To the Editor:—The controversy with regard to Demerol appearing in the Correspondence department of The Journal of September 7 has been followed attentively by the Italian medical public.

Demerol in the form of the hydrochloride of methyl-phenyl-piperidyl ethyl carbonate is well known in Europe and has been largely used in Italy. Controversies such as now appear in The Journal on the more or less narcotic character of the drug have happened in Europe. In Germany it was finally decided to list the new preparation among the narcotics and to impose the same regulations on the medical practitioner as were in force for morphine. But in Italy the product has never been classed as a narcotic, and till a few months ago it could be obtained without license from the druggist, as opposed to narcotics. Actually in Italy the product commands a very high price per vial in the black market, but no special prescription (as in the case of morphine) is required from a medical practitioner.

In spite of all the laboratory assertions, use of the drug from 1939 to 1945 has taught us that addiction is also produced with it. We are therefore fully in accord with the authoritative declaration of Dr. Anslinger. But this addiction is less troublesome than that due to morphine, in that it is not so general. Patients with renal colic have come happily through the operation and recovered quickly from "addiction" though used to ten or more vials of Dolantin per day, a phenomenon that is never shown by morphine. Probably it is really due to the chemical relationship with atropine that addiction to it is "selective" among the patients.

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Naples, Italy.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Privileged Communications: Applicability of Statute to Physicians and Inmates of State Hospital for Insane.—Claimant, a minor, by his guardian, filed suit against the state of New York for damages arising from his having been assaulted by a fellow inmate at the Harlem Valley State Hospital, an institution owned and operated by the state of New York for the observation, treatment and care of the mentally ill. The case was heard in the court of claims of New York.

The claimant and one Benturira had been patients in the Harlem Valley State Hospital for some years prior to the date of the assault, the claimant with a diagnosis of psychosis with mental deficiency and Benturira with a diagnosis of psychosis and epileptic clouded states. On the date of the assault, both individuals had been confined to their beds by means of restraint sheets in the restraint room, which formed part of the ward reserved for the care of the more violent inmates. At about 1:45 a. m. Benturira succeeded in breaking out of his restraint sheet and brutually attacking the claimant, who was still confined and unable to defend himself. As a result of this attack the claimant suffered a fractured nose and various bruises and was rendered permanently blind. At the trial claimant endeavored to introduce into evidence the hospital record of Benturira, contending that this record would clearly establish that the officers and employees of the hospital well knew that Benturira was of a violent and assaultive disposition and that he had escaped from restraint sheets on several occasions. The conclusion sought to be drawn was that in the light of this knowledge the officers and employees were negligent in permitting these two inmates to be confined in the same room without special precautions. The state objected to the introduction of this record on the ground that its contents were privileged communications between the hospital physicians and the patient, within the meaning of section 352 of the civil practice act.

Section 352 of the civil practice act provides, in substance, that a physician shall not be allowed to disclose any information he acquired in attending a patient in a professional capacity and which was necessary to enable him to act in such capacity. It has already been held, the court pointed out, that this professional relationship does not exist between the official physicians of a state hospital and its inmates. In Wigmore on Evidence (ed. 3, section 2285) four fundamental conditions necessary to the establishment of a privilege against the disclosure of communications are set forth: (1) The communications must originate in a confidence that they will not be disclosed; (2) such confidence must be essential to the satisfactory maintenance of the relationship; (3) the relationship must be one which ought to be sedulously fostered; and (4) the injury resulting from disclosure must be greater than the benefit disclosure would afford in disposing of litigation correctly. The privilege here asserted by the state, said the court, fails to meet any of these tests excepting the third. It is extremely dubious that John Benturira considered any communications to the hospital physicians, or any observations made by them, as confidential, and it is difficult to see how either confidentiality or its lack would affect the relationship between such physicians and a mentally deficient patient. Further, any conceivable injury to such relationship resulting from the disclosure of the records at this trial is certainly outweighed by the value of such disclosure in arriving at an informed decision in the case.

Continuing, the court said that, even assuming that the privileged relationship of physician and patient might exist in such an institution, an exception to the privilege appears to be provided by section 84 of the mental hygiene law. This section, after discussing the type of records which must be made relative to the inmates of such institutions, provides:

> Such record shall be accessible only to the director and such officers and subordinates of the institution as he may designate and to the commissioner and his representatives, except on the consent of the commissioner or an order of a judge of a court of record.

Certainly, said the court of claims, in the light of this section, the hospital records of an inmate of a state institution for the care of the mentally ill enjoy no such absolute privilege against disclosure that only the patient can waive it, as is now contended by the state. The section clearly provides that such records may be disclosed to any one, without consulting the patient, on the consent of the commissioner or on the order of a court of record. This court made an order on the claimant's motion directing the state of New York through its physicians and employees to submit to an examination before trial with respect to, among other things, the diagnosis, treatment, care and conduct of John Benturira and also directing the state to submit, for discovery and inspection by the claimant and his attorneys, substantially all of its record relating to the same matter. This order of examination and discovery was such an order of a court of record as is contemplated by section 84 of the mental hygiene law. At the time when this order was under consideration the state not only did not oppose but consented to those portions thereof concerning the examination and inspection with respect to Benturira and did subsequently submit to a lengthy and detailed examination before trial with respect to the diagnosis, treatment, care and conduct of John Benturira and did submit for inspection all of the now disputed records concerning him. No question of privilege with respect to such records was raised by the state at the time when the order was granted, no appeal was taken from the order, and no objections to any questions concerning Benturira were made during the examination. Such conduct on the part of the state would seem to amount to a waiver of the right to claim the benefit of the privilege. It seems adequately established that waiver of the privilege may be implied as well as expressed; that it may be implied from conduct not only at the trial but also in an examination preliminary thereto; and that voluntary disclosures on such a preliminary examination may be given the same effect as formal waiver on the trial. Accordingly the court of claims concluded that the relationship of physician and patient does not exist between state hospital physicians and mentally deficient inmates to the extent that communications between them are absolutely barred from disclosure by section 352 of the civil practice act and that such privilege as may exist under some circumstances is limited by section 84 of the mental hygiene law. This and other contentions having been resolved in favor of the plaintiff, judgment was entered therefor.—*Scolavino v. State, 62 N. Y. S. (2d) 17 (N. Y., 1946).*

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of the boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Jan. 11, page 125.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part III.* Durham, Oct. 21-23. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Los Angeles, April 11-12. Sec., Dr. P. M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Various centers, March 24. Final date for filing application is Feb. 17. *Oral.* New York City, April 25-27. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Chicago, March 17. *Oral.* Chicago, April 24-26. Final date for filing application is Feb. 15. Asst. Sec., Dr. W. A. Werrell, 1 W. Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY. *Oral.* Examination to be given during the Summer. Applications for examination will be accepted until Feb. 15. Sec., Dr. P. C. Bucy, 912 S. Wood St., Chicago.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part II.* Pittsburgh. June 1-7. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral. All Groups. Parts I and II.* Chicago, October 1947. Final date for filing application is March 1. Sec., Dr. S. J. Beach, 56 Ivie Rd., Cape Cottage, Me.

AMERICAN BOARD OF ORTHOPEDIC SURGERY: Applications for the next examination for Part I will be accepted until Feb. 1. Sec., Dr. Francis M. McKeever, 1136 W. Sixth St., Los Angeles 14.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* St. Louis, April 16-19. Chicago, Oct. 7-11. Sec., Dr. D. M. Lierle, University Hospitals, Iowa City, Ia.

AMERICAN BOARD OF PATHOLOGY: Philadelphia, June 3-4. Final date for filing application is April 15. Sec., Dr. Robert A. Moore, Euclid Ave. and Kings Highway, St. Louis 10.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1937 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Clinical Pathology, Baltimore

16:597-670 (Oct.) 1946

Present Status of Rh Factor. P. Levine.—p. 597.
Contrast Coloring of Media by Dyes in Growing Tubercle Bacilli: Effect of Dyes on Growth of Tubercle Bacilli. H. J. Corper and M. L. Cohn.—p. 621.
*Reactions of Tissue to Cold: Pathology of Frostbite, High Altitude Frostbite, Trench Foot and Immersion Foot. N. B. Friedman.—p. 634.
Cirrhosis of Liver and Diabetes as Related to Hemochromatosis. P. A. Herbut and H. T. Tamaki.—p. 640.
Glycogen Storage Disease of Heart. J. L. Haymond and A. S. Giordano. —p. 651.

Reactions of Tissue to Cold.—Friedman discusses the pathologic anatomy and pathogenesis of local injury due to cold on the basis of a study of material collected at the Army Institute of Pathology during World War II. Essential dissimilarity between the lesions of trench foot and of high altitude frostbite was not found. Agglutinative thrombosis resulting in ischemic gangrene can account for the most severe lesions, but some of the changes, particularly those in lipoid rich tissues, may be due to cold directly.

Annals of Otol., Rhin. and Laryngology, St. Louis

55:467-714 (Sept.) 1946. **Partial Index**

Osteomyelitis of Maxilla Secondary to Suppurative Maxillary Sinusitis. H. I. Lillie.—p. 495.
Danger of Unrecognized Anoxia in Laryngology. T. C. Galloway. —p. 508.
Intranasal Medication: Investigation into Relative Merits of Certain Methods of Introducing Fluids into Nose. T. Cawthorne.—p. 519.
Aphonia. C. H. McCaskey.—p. 524.
Intralaryngeal Operation for Cancer of Vocal Cord. F. E. LeJeune. —p. 531.
Endaural Approach to Mastoid for Complete Mastoidectomy, with Report of 43 Operations. G. L. Boyden.—p. 543.
Associated Paralyses of Larynx. C. C. Cody Jr.—p. 549.
Aids in Rhinoplastic Procedures. O. J. Becker.—p. 562.
Cleft Palate. H. G. Beatty.—p. 572.
Rhinosporidiosis. F. R. Spencer.—p. 580.
Tonsillectomy and Poliomyelitis. D. S. Cunning.—p. 583.
Tonsillectomy and Poliomyelitis. E. R. Roberts.—p. 592.

Archives of Dermatology and Syphilology, Chicago

54:377-496 (Oct.) 1946

*Eczematous and Pigmentary Lichenoid Dermatitis: Atypical Lichen Planus: Preliminary Report. D. J. Wilson.—p. 377.
Neurodermatitic Reaction. W. Sachs, C. S. Miller and Margaret B. Gray.—p. 397.
Study on Ulcus Phagedenicum Cutis. A. Dostrovsky and F. Sagher. —p. 408.
Vitamin B Complex in Treatment of Lichenoid Dermatitis. E. S. Bereston and G. Cheney.—p. 425.
Progressive Recurrent Dermatofibroma (Darier-Ferrand): Anatomoclinical Study. O. G. Costa.—p. 432.

Eczematous and Pigmentary Lichenoid Dermatitis.—Wilson reports more than 300 cases of lichenoid dermatitis. The disease is protean in its manifestations. At first it was thought that it arose only in New Guinea, but it was observed also in the Mediterranean region. The eruptions can be divided into the dry type, comprising approximately 20 per cent of the cases from the Southwest Pacific, and the exudative type, comprising 80 per cent. Either type may be mild or severe, and both may present complications. The two types may be present in the same person and at the same time. In some cases the lesions first are dry and then become eczematous and again are dry. The cause is not known, although several factors are probably involved, including low vitamin intake, especially vitamin A, quinacrine hydrochloride (atabrine) and allergy. It is believed that vitamin A deficiency predisposes to the disease but that quinacrine hydrochloride is the major factor.

Archives of Ophthalmology, Chicago

36:387-530 (Oct.) 1946

Congenital Encephalo-Ophthalmic Dysplasia. A. C. Krause.—p. 387.
Etiology and Treatment of Blepharitis: Study in Military Personnel. P. Thygeson.—p. 445.
*Retrobulbar Neuritis and Complete Heart Block Caused by Digitalis Poisoning: Report of Case. H. P. Wagener, H. L. Smith and R. W. Nickeson.—p. 478.
Exposure and Fixation of Eye in Early Days of Cataract Extraction. B. Chance.—p. 484.

Digitalis Poisoning.—Wagener and his associates observed digitalis poisoning in a man aged 50 who came to the Mayo Clinic because of poor vision, generalized weakness, nausea and vomiting. Two or three months previously he had had extrasystoles and had been given "leaf medicine" one tablet four times daily for about two weeks. After two weeks his medicine had been changed to another "green digitalis tablet"; he had taken one tablet three times daily for six weeks. About two weeks before he came to the clinic his appetite had become poor and he had vomited several times. He had noticed that lights had become yellow and that green grass had assumed a yellow tint. His vision had also become blurred, and he had found himself unable to read. Bilateral central scotomatous defects were demonstrated in the fields of vision, and complete heart block was demonstrated by electrocardiography. The vision returned to normal in about five weeks without treatment except for withdrawal of the digitalis and increasing the amount of fluid ingested by mouth.

Bull. of the U. S. Army Med. Dept., Washington, D. C.

6:347-490 (Oct.) 1946

Closed Head Injury Syndrome Due to Blast. J. A. Aita and W. Z. Kerman.—p. 411.
Modern Technics for Studying Hemolytic Streptococci. H. F. Swift. —p. 428.
Abdominal Wounds in Western Desert. W. H. Ogilvie.—p. 435.
Japanese Military Psychiatry in Korea. M. M. Berger.—p. 445.
Armored Division Personnel Adjustment Plan. J. F. Zigarelli.—p. 449.
Tuberculosis in Army in North Africa and Italy. G. T. McKean and D. S. King.—p. 452.
Observations on Infectious Hepatitis in Seventh Army, 1944-1945. H. Gowen.—p. 456.
Acrylic Moist Chamber Spectacles and Pinhole Glasses. J. W. Hallett and S. Pittler.—p. 462.
Pressurized Oxygen Therapy: Case Report. J. C. Shrader and N. Kaliss.—p. 466.

Cancer Research, Baltimore

6:593-656 (Nov.) 1946

Effect of Nitrogen Mustards on Viscosity of Thymonucleate. E. C. Gjessing and A. Chanutin.—p. 593.
Effect of Nitrogen Mustards on Ultraviolet Absorption Spectrum of Thymonucleate, Uracil and Purines. A. Chanutin and E. C. Gjessing. —p. 599.
Introduction of Neoplasia in Vitro with Virus: Experiments with Rabbit Skin Grown in Tissue Culture and Treated with Shope Papilloma Virus. D. R. Coman.—p. 602.
Effect of Progesterone on Development of Mammary Cancer in C3H Mice. H. Burrows and Cornelia Hoch-Ligeti.—p. 608.
Influence of Sex Hormones on Hepatic Lesions Produced by 2-Acetylaminofluorene. A. Cantarow, K. E. Paschkis, J. Stasney and M. S. Rothenberg.—p. 610.
Tumors of Salivary and Parathyroid Glands in Rats Fed with 2-Acetylaminofluorene. J. Heiman and Doris Meisel.—p. 617.
Localization of Stratum of Maximum Mitotic Frequency in Epidermal Methylcholanthrene Carcinogenesis in Mice. E. V. Cowdry, J. H. Van Dyke and B. B. Geren.—p. 620.
Further Studies of Specific Precipitin Antiserums for Protein of Cancer Tissue: III. Relation of Proteins of Different Malignant Tissues to Each Other. L. S. Mann and W. H. Welker.—p. 625.
Transplantable 9,10-Dimethyl-1,2-Benzanthracene Sarcoma in Syrian Hamster. E. D. Crabb.—p. 627.

Georgia Medical Association Journal, Atlanta

35:243-272 (Sept.) 1946

Psychosomatic Gynecology. J. P. Pratt.—p. 243.
Psychosomatic Aspects of Problem Cases in Medicine and Surgery. J. M. Barnett.—p. 250.
Man versus the Ameba. A. H. Bunce.—p. 256.

Journal of International College of Surgeons, Chicago

9:511-654 (Sept.-Oct.) 1946

Surgical Treatment of Cancer of Rectum and Pelvic Colon Without Colostomy and with Preservation of Sphincter Muscles. H. E. Bacon, J. P. Fleming, C. H. Smith and M. B. Holoman.—p. 511.
Transplantation of Ureters to Bowel. E. Hess.—p. 517.
Experiments with "Cuto-Omentopexy" and Skin Homotransplantation. F. Mandle and N. Rabinovici.—p. 525.
Simple, Thorough Operative Technic for Excochleation of Disk Herniation. T. Kalima.—p. 531.
Carcinoma of Breast. H. Acuff.—p. 536.
Intra-Abdominal Plastic Repair. W. S. Bainbridge.—p. 542.
Phlebitis, Embolism and Thrombosis. M. Behrend.—p. 552.
Some Items on Treatment of Urethral Strictures: Simplified Operative Method for Impassable Strictures. J. Bitschai.—p. 559.
Late Effect of Radiotherapy on Intestine. A. O. Wilensky.—p. 579.
Treatment of Chronic Osteomyelitis. H. L. Puckett.—p. 581.
Management of Cholecystitis. C. D. Brooks, H. W. Ulch, P. J. Connelly and J. F. Kelly.—p. 589.
Surgical Treatment of Varicose Veins. S. H. Babington.—p. 596.
Gynecomastia: New Surgical Technic. E. F. Malbec.—p. 652.

Journal of Lab. and Clinical Medicine, St. Louis

31:1053-1164 (Oct.) 1946

*Demonstration of Rh Antibodies in Newborn and Further Evidence of Pathogenesis of Erythroblastosis. J. M. Hill and S. Haberman.—p. 1053.
Blood Transfusion Studies: I. Differentiation of Hemolytic and Nonhemolytic Transfusion Reactions. E. B. Flink.—p. 1067.
Id.: II. Survival of Fresh and Stored Transfused Erythrocytes as Determined by Urobilinogen Excretion. E. B. Flink and K. B. Skubi.—p. 1074.
*Blood and Bone Marrow in Infectious Mononucleosis: Review of Literature and Report of 25 Cases. L. R. Limarzi, J. T. Paul and H. G. Poncher.—p. 1079.
Preservatives for Syphilitic Serum, with Special Reference to Use of Merthiolate. C. C. Croft and Lucia L. Smith.—p. 1101.
Secondary Bacillus Pyocyaneus Infection in Meningitis Following Intrathecal Penicillin Therapy. Ruth C. Harris, Lillian Buxbaum and E. Appelbaum.—p. 1113.
Two Dose Dextrose Tolerance Test in Diagnosis of Diabetes Mellitus. J. F. Conner and F. W. Reynolds.—p. 1121.
Detailed Report on Weights and Weight Losses of 24 Men in Santo Tomas Internment Camp. B. H. Brown.—p. 1129.
Comparative Efficiency of Various Liver Function Tests in Detecting Hepatic Damage Produced in Dogs by Xylidine. J. L. Svirbely, A. R. Monaco and W. C. Alford.—p. 1133.
Study of Absorption from Crystalline Insulin Pellets and Solutions at Various Sites in Rabbits. R. C. Page and E. H. Lang.—p. 1144.
Nature of Action of Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl): Effects on Human Eye. R. Harris, T. H. McGavack and H. Elias.—p. 1148.

Rh Antibodies in Newborn and Pathogenesis of Erythroblastosis.—Hill and Haberman report 10 cases of erythroblastosis in newborn infants which showed relatively good correlation between severity of the disease and antibody titer as demonstrated by the developing test. By using anti-human globulin serum as a routine developing test in suspected Rh isoimmunizations the advantages of this test in respect to its sensitivity for incomplete antibodies were confirmed and its usefulness in demonstrating Rh antibody in the serum of mother and infant was proved. This test also detects specific Rh antibodies not demonstrable with agglutinating or blocking tests. The developing test as applied to the demonstration of adsorbed antibodies on fetal erythrocytes is suggested as a diagnostic test for erythroblastosis. Immediate and adequate transfusion of Rh-negative blood is recommended for hemolytic disease of the newborn. Breast feeding is contraindicated when Rh antibodies can be demonstrated in the maternal or fetal serum or adsorbed on fetal erythrocytes.

Blood and Bone Marrow in Infectious Mononucleosis.—Limarzi and his associates report 25 cases of infectious mononucleosis in 18 men and 7 women between the ages of 13 months and 35 years. The characteristic finding in the differential count was the large number of abnormal "leukocytoid" lymphocytes in the peripheral blood. In spite of this the bone marrow showed a lack of lymphocytic infiltration and replacement of the marrow by lymphocytes seen in cases of lymphatic leukemia. The bone marrow revealed a myeloid hyperplasia and immaturity. Either the "toxic agent" acts on the bone marrow to produce a myeloid hyperplasia and suppresses their delivery to the peripheral blood or the suppression of the myeloid tissue results in a myeloid hyperplasia. Sternal puncture is of aid in the differential diagnosis of benign and malignant types of lymphocytosis.

Journal-Lancet, Minneapolis

66:351-398 (Nov.) 1946

John Charnley McKinley: Personal Appreciation. J. A. Myers.—p. 351.
War Psychiatry and Its Influence on Postwar Psychiatry and on Civilization. E. A. Strecker.—p. 357.
*What Do We Know of Multiple Sclerosis? H. H. Reese.—p. 359.
Brain Changes Associated with Electrical Shock Treatment: Critical Review. B. J. Alpers.—p. 363.
Note on Development of Speech Patterns. R. R. Grinker.—p. 370.
Neuritis Ossificans with Osteogenic Sarcoma in Brachial Plexus Following Trauma: Report of Case. H. W. Woltman, A. W. Adson and K. H. Abbott.—p. 372.
The Psychiatrist Looks at Family Life. D. D. Bond.—p. 377.
Endogenous Toxic Encephalitis. A. B. Baker and D. Daly.—p. 381.
*Occlusions of Arteries Supplying the Brain Stem and Cerebellum. J. E. Skogland.—p. 385.
Psychiatric Care in Hospitals. L. R. Gowan.—p. 389.
Huntington's Chorea in Relation to Heredity of Personality Disorders. B. C. Schiele.—p. 393.

Multiple Sclerosis.—Reese reports 241 cases of multiple sclerosis, 65 of which were studied over a long period. Blood studies revealed a definite tendency to a higher eosinophilia, though allergic signs in history and clinical examination were lacking. Practically all the patients presented a starting hypoprothrombocytopenia. The anticoagulant Dicumarol (3-3'-methylene-bis-[hydroxycoumarin]) was used in 28 cases for from two months to over one and a half years, but no objective improvement was seen. Horton's histamine treatment has given satisfactory results in early and remittent cases of multiple sclerosis. Each case must be tried on rationally acceptable therapeutic schemes, since no specific therapy is available.

Vascular Lesions of Brain Stem and Cerebellum.—Skogland reports 8 cases of clinical syndromes associated with thrombosis of arteries supplying the brain stem and cerebellum in patients who were admitted to the Charity Hospital in New Orleans during the period 1935 to 1943. There were 4 patients presenting the syndrome of the posterior inferior cerebellar artery, 1 with thrombosis of the vertebral artery and 3 with thrombosis of the basilar artery. Cases of thrombosis of the anterior spinal artery and of the superior cerebellar artery are reported in the literature, but there were no admissions of persons thus affected to the Charity Hospital. The close correlation between clinical symptoms and distribution of pathologic changes is emphasized.

Journal of National Malaria Society, Tallahassee, Fla.

5:95-168 (June) 1946

Postwar Malaria Control in Continental United States. M. D. Hollis.—p. 95.
Species Eradication by Means of DDT. H. H. Stage.—p. 99.
*Malaria Mortality and Morbidity in United States for Year 1944. E. C. Faust, A. D. Hess and M. D. Young.—p. 103.
Recent Developments in Use of DDT and Other Mosquito Insecticides and Repellents. E. F. Knipling.—p. 113.
Effect of Deficiencies in Vitamins and in Protein on Avian Malaria. A. O. Seeler and W. H. Ott.—p. 123.
Observations on Bionomics of Principal Malaria Vector in New Hebrides-Solomon Islands. W. J. Perry.—p. 127.
Entomologic Evaluation of DDT Residual Spraying for Malaria Control. G. H. Bradley and R. F. Fritz.—p. 141.
Apparent Anomalies in Behavior of Anopheline Mosquitoes in Southwestern Georgia. O. K. Fletcher Jr.—p. 147.
Experimental Transmission of P. Falciparum by Anopheles Maculipennis Freeborni. R. W. Burgess and M. D. Young.—p. 151.
Three New Anopheline Records from New Guinea. W. V. King and H. Hoogstraal.—p. 153.
Progress in Development of Malaria Control Technics. S. W. Simmons.—p. 157.
*Plasma Quinacrine Concentrations Attained by Subjects Taking 0.1 Gm. of the Drug Daily. E. R. Becker, C. S. Burks and E. Kaleita.—p. 165.

Malaria Mortality and Morbidity.—Faust and his associates present the yearly assessment of the status of malaria in the United States for 1944, based on replies received from a questionnaire sent to the bureau of vital statistics of the forty-eight states. The picture continues to be more favorable every year. The endemic regions in the South have shrunken within the last five years. Malaria deaths outside the South are becoming less frequent, and of those certified the majority have resulted from exposure in the South or outside the United States. However, civilian infections reported to state boards of health do not adequately reflect the malariousness of the respective area. Few states have records approximating the actual number of cases of malaria existing within their

area. Few state agencies carried out malaria or antimosquito campaigns in 1944. The discharge to civilian life of military forces with recurring vivax malaria may constitute a serious public health hazard in areas where Anopheles mosquitoes are allowed to breed in numbers, unless antimosquito campaigns continue to be vigorously prosecuted.

Plasma Quinacrine Concentrations.—Military personnel in the vicinity of Ledo, Assam, India, were placed on a suppressive quinacrine regimen of 0.1 Gm. daily (0.7 Gm. per week). Twenty-one volunteers were selected as subjects whose quinacrine concentration of the plasma could be followed. None had taken quinacrine previously. The mean plasma quinacrine levels of 14 of these 21 stabilized within two weeks at values ranging from 21.3 to 26.0 micrograms per liter. Seven others attained somewhat lower means, apparently because this group contained 4 persons who might be called "poor absorbers." None of these 21 exhibited extraordinarily high levels, but in other studies a number of such persons were encountered and most of these showed extreme coloring of the skin.

Journal of Nervous and Mental Disease, New York

104:351-464 (Oct.) 1946

Influence of Emotion on Human Electroencephalogram. R. Cohn.—p. 351.
Combat Exhaustion. L. H. Bartemeier, L. S. Kubie, K. A. Menninger, J. Romano and J. C. Whitehorn.—p. 358.
Closed Head Injury Syndrome Due to Blast. J. A. Aita and W. Z. Kerman.—p. 390.
Criteria for Stages of Pentothal Anesthesia. H. E. Himwich and B. Etsten.—p. 407.
Evaluation of Therapeutic Role of Narcoanalysis in Mental Disorders. D. A. Barbara.—p. 414.
Schistosomiasis of Central Nervous System. J. G. Cutler.—p. 425.
*Porphyria: Neuropsychiatric Aspects in Case of Negro. J. M. Schneck. —p. 432.

Neuropsychiatric Aspects of Porphyria. — Schneck reports that a Negro soldier aged 40 began unexplainably to experience anxiety when in crowds. Later he developed impairment of vision. Concurrent with episodes of weakness accompanied with impaired vision there would be excretion of urine which appeared a deep orange and at times red. Constipation developed. Neurologic examination revealed generalized hyperactive reflexes, except for the absence of knee jerks, which reappeared on repeated tapping of the tendon. An especially interesting fact in the reported case is the sequential relationship of the anxiety episodes to the onset of the physical manifestations of porphyria.

Journal of Nutrition, Philadelphia

32:227-344 (Sept.) 1946

Retention of Nutrients in Cheese Making: IV. Thiamine in Cheddar Cheese Made from Raw and Pasteurized Milk. E. V. Evans, O. R. Irvine and L. R. Bryant.—p. 227.
*Reproductivity and Growth of Albino Rats on Prolonged Daily Intake of Caffeine. G. Bachmann, J. Haldi, W. Wynn and C. Ensor.—p. 239.
Metabolism of Women During Reproductive Cycle: VIII. Utilization of Thiamine During Lactation. Charlotte Roderuck, H. H. Williams and Icie G. Macy.—p. 249.
Id.: IX. Utilization of Riboflavin During Lactation. Charlotte Roderuck, Margaret N. Coryell, H. H. Williams and Icie G. Macy.—p. 267.
Self Selection of Diet: III. Appetites for B Vitamins. E. M. Scott and Eleanor Quint.—p. 285.
Id.: IV. Appetite for Protein. E. M. Scott and Eleanor Quint.—p. 293.
Protein Concentrates as Amino Acid Sources for the Chick: Corn Gluten Meal, Cottonseed Meal and Peanut Meal. C. R. Grau.—p. 303.
Nutritive Value of Protein of Varieties of Legumes and Effect of Methionine Supplementation. W. C. Russell, M. Wight Taylor, Thalia G. Mehrhof and Renate R. Hirsch.—p. 313.
Influence of Single Dose of Alpha Tocopherol Administered to Vitamin E Deficient Rats on Fifteenth Day on Subsequent Growth. H. Kaunitz. —p. 327.
*Evidence of Citric Acid Synthesis in Human Subjects. Juniata E. Strom and Milicent L. Hathaway.—p. 337.

Reproductivity of Rats Given Caffeine.—Albino rats were given a sweetened caffeine beverage as their sole source of fluid throughout their reproductive period. The reproductive capacity as judged by the number of litters and number of offspring was not impaired by the daily ingestion of caffeine.

Evidence of Citric Acid Synthesis in Human Subjects. —Strom and Hathaway maintained 3 normal women for forty-five days on a synthetic diet free from citrates and for twenty-one days on a controlled natural food diet of similar nutritive value but supplying approximately 797 mg. of citric acid daily. Individual variations in daily citrate excretion of 300 to 500 mg. were found on both the synthetic and the natural food diets. These and other observations convinced the authors that citrates in the urine are largely synthesized by tissues rather than coming from body stores.

32:345-466 (Oct.) 1946

*Role and Efficiency of Animals in Utilizing Feed to Produce Human Food. L. A. Maynard.—p. 345.
Adequacy of Intravenous Partial Acid Hydrolysates of Casein and Fibrin for Nitrogen Balance in Dogs. D. V. Frost and W. C. Risser. —p. 361.
Vitamin B. Complex Studies with Diets Differing in Carbohydrate Component. H. R. Skeggs and L. D. Wright.—p. 375.
Further Experiments on Relation of Fat to Economy of Food Utilization: I. By the Growing Albino Rat. E. B. Forbes, R. W. Swift, W. H. James and others.—p. 387.
Further Experiments on Relation of Fat to Economy of Food Utilization: II. By the Mature Albino Rat. E. B. Forbes, R. W. Swift, E. J. Thacker and others.—p. 397.
Dental Caries in Cotton Rat: VIII. Further Studies on Dietary Effects of Carbohydrate, Protein and Fat on Incidence and Extent of Carious Lesions. B. S. Schweigert, Elizabeth Potts, J. H. Shaw and others. —p. 405.
Utilization of Calcium in Soybean Products and Other Calcium Sources. L. J. Schroeder, W. M. Cahill and A. H. Smith.—p. 413.
Vitamin B6 and Its Relation to Beta-Pyracin Lactone in Metabolism of Chick. C. J. Campbell, R. A. Brown, O. D. Bird and A. D. Emmett. —p. 423.
Nutritive Value of Canned Foods: Changes in Vitamin Content of Foods During Canning. N. B. Guerrant, M. G. Vavich, O. B. Fardig and others.—p. 435.
Diet of Mother and Hydrocephalus in Infant Rats. L. R. Richardson and A. G. Hogan.—p. 459.

Efficiency of Animals to Produce Human Food.—Maynard shows that, while the feeding of animals results in a concentration of food nutrients into more palatable and more digestible forms for human use, it also involves wastage. Adjustment of livestock production in the interests of better nutrition for more people should recognize differences among species and feeding operations with respect to (*a*) efficiency of human food production, (*b*) consumption of foods directly useful to man and (*c*) nutritive value of the animal product. Taking these factors into account, it is concluded that milk production should have first priority on feed supplies available. Butter production rates the same priority only to the extent that the skim milk is recovered for human use. Egg production should be ranked above pork production, but broiler production deserves only a low rating. To the extent that beef cattle and sheep utilize range and other roughage not available to dairy cattle, their production should have a high priority rating, but heavy fattening of meat animals is an inefficient use of the basic food supply in relation to human needs.

Journal of Pediatrics, St. Louis

29:417-540 (Oct.) 1946

*Histoplasmin Sensitivity. A. Christie and J. C. Peterson.—p. 417.
Electrophoretic Patterns of Blood Sera in Poliomyelitis and Guillain-Barré's Disease (Encephalomyeloradiculitis). V. C. Kelley, D. R. Briggs and R. A. Jensen.—p. 433.
Baby Grid: Application of Grid Technic to Growth and Development in Infants. N. C. Wetzel.—p. 439.
Effect of Diabetic and Prediabetic Pregnancies on Fetus and Newborn Infant. H. C. Miller.—p. 455.
*Kernicterus in Erythroblastosis Fetalis. V. C. Vaughan.—p. 462.
Importance of Chronologic Records in Management of Allergic Children. A. B. Schwartz.—p. 474.
Nonrachitic Bowlegs in Childhood: Osteochondrosis Deformans Tibiae. D. W. Leonard and L. Cohen.—p. 477.
Influenza Virus Vaccine: Local and Systemic Reactions in Children. H. B. Grant.—p. 485.
*Immune Response to Early Administration of Pertussis Vaccine. W. W. Waddell Jr. and C. S. L'Engle Jr.—p. 487.
Parapertussis Pneumonia: Report of 2 Fatal Cases. W. W. Zuelzer and W. E. Wheeler.—p. 493.
Mistreatment of Congenital Hemolytic Disease (Erythroblastosis Fetalis) by Transfusions of Rh-Positive Blood and Maternal Serum: Case Report. A. S. Wiener and M. A. Hyman.—p. 498.
Erythroblastic Anemia of Cooley: Observations on Effect of Splenectomy Performed on Identical Twins. C. D. Govan.—p. 504.
Erythema Multiforme, with Special Emphasis on Postvaccinal Erythema. M. H. Schwartz and H. D. Brainerd.—p. 512.
Case of Erythroblastosis Fetalis Caused by Isoimmunization with Agglutinogen. B. S. Gruber, A. Litvak and M. Jacobi.—p. 518.
Transfusion of Very Small Infants, Utilizing Pneumatic Pressure. E. F. Patton.—p. 520.

Histoplasmin Sensitivity. — Christie and Peterson performed more than 2,000 histoplasmin tests in various age groups and from a considerable area of the country, including Tennessee, various of the Southeastern states, Pennsylvania, New Jersey

and New York. The age relationships in the development of histoplasmin sensitivity, pulmonary calcifications and tuberculin sensitivity and the geographic variations of histoplasmin sensitivity, pulmonary calcifications and tuberculin sensitivity are presented. The significance of histoplasmin sensitivity as demonstrated in these studies and the significance of these studies in relationship to the study of the epidemiology of tuberculosis are discussed.

Kernicterus in Erythroblastosis Fetalis.—Vaughan reports 72 cases of erythroblastosis fetalis with 25 deaths. Necropsy was performed in 21 cases. Four of the surviving patients had mental retardation. An unfavorable outcome was associated with the clinical or pathologic signs of kernicterus in 20 cases. In 12 cases of kernicterus there were also focal pulmonary hemorrhages, and these infants displayed a striking clinical picture made up variously of drowsiness, spasticity, opisthotonos, signs of motor irritability, respiratory irregularity, pulmonary rales and rhonchi, and bloody discharge from the upper respiratory tract. Clinical and pathologic features of the cases in which kernicterus was present suggest that blood destruction is not the primary determinant of nuclear damage. Immaturity, vascular injury, altered antigen-antibody reactivity and intrapartum transfer of antibody may play possible roles in the pathogenesis of kernicterus.

Pertussis Vaccine.—Waddell and L'Engle administered deep subcutaneous injections of 0.5 cc. of a vaccine containing 40,000 million killed whooping cough bacilli (phase I) to 129 infants 1 week of age, with a second dose of 1 cc. at 1 month of age and a third dose of 1 cc. at 2 months of age. In order to determine the advisability of a booster dose, 1 cc. of vaccine was administered to 50 previously vaccinated infants at approximately 6 months of age and the agglutinin titer determined one week later. Results showed that it is advisable to start immunization against pertussis from six weeks to two months after birth. A booster dose at seven to eight months may well be given as an added measure of precaution. A satisfactory immune response can be regularly expected when a first dose of pertussis vaccine is administered in the neonatal period. Pertussis vaccine can be safely administered at this early age period without fear of disagreeable local or systemic reactions.

Journal Pharmacology & Exper. Therap., Baltimore

88:109-194 (Oct.) 1946

Effect of Carbon Tetrachloride Induced Liver Injury on Acetylcholine Hydrolyzing Activity of Blood Plasma of Rat. R. W. Brauer and Mary A. Root.—p. 109.
Pharmacology of Penicillic Acid. M. F. Murnaghan.—p. 119.
Hemolytic Anemia as Manifestation of Paraphenylenediamine Toxicity. J. E. Davis.—p. 133.
Antagonism of Tetraethylammonium Against Heart Depressants. O. Loewi. —p. 136.
Relation of Plasma Concentration of Quinacrine to Its Antimalarial Activity. E. K. Marshall Jr. and E. H. Dearborn.—p. 142.
Studies on Pharmacology and Acute Toxicity of Compounds with Marihuana Activity. S. Loewe.—p. 154.
Correlation Between Distribution of Antimony in Tissues and Chemotherapeutic Effect in Experimental Leishmaniasis. A. Gellhorn and H. B. van Dyke.—p. 162.
Some Toxicologic and Pharmacologic Properties of Citrinin. A. M. Ambrose and F. DeEds.—p. 173.
Comparison of Drug Diet Therapy with Single Daily Oral Dosage in Avian Malaria. E. K. Marshall Jr. and E. H. Dearborn.—p. 187.
Effect of Chloroform and Ether on Activity of Cholinesterase. O. Miquel. —p. 190.

Nebraska State Medical Journal, Lincoln

31:389-432 (Oct.) 1946

Urologic Complications of Pregnancy and Labor. R. McCaffery and E. Hess.—p. 392.
Syphilis and Penicillin Therapy. A. C. Curtis.—p. 402.
Progress in Elimination of Permanent Colostomies in Carcinoma of Rectum and Rectosigmoid. R. R. Best.—p. 406.
Cancer Control Program. J. F. Kelly.—p. 412.
Proceedings of Staff, Nebraska Methodist Hospital, J. R. Schenken, Editor: III. Congenital Atresia of Bile Ducts. C. Moore.—p. 415.

31:433-476 (Nov.) 1946

Acute Hepatitis in Civilian Practice. G. B. Eusterman.—p. 436.
Experiences with Late Trench Foot and Frostbite. T. J. Dry.—p. 443.
Medical Management of Graves' Disease. F. Rogers.—p. 447.
Gastrointestinal Allergy. M. H. Brodkey.—p. 451.
Venereal Disease Control in Rural Area. W. B. Quisenberry and J. N. Dudley.—p. 456.

New England Journal of Medicine, Boston

235:501-532 (Oct. 3) 1946

Therapeutic Score Card for Rheumatoid Arthritis: Standardized Method of Appraising Results of Treatment. O. Steinbrocker and A. Blazer. —p. 501.
Chiari's Syndrome: Report of Case. H. L. Hirsh and B. Manchester. —p. 507.
Recurrent Spontaneous Emphysema of Mediastinum with Concomitant Pneumothorax: Report of Case. J. D. Schendstok.—p. 511.
Unilateral Tremor of Lower Extremity: Its Association with Internal Derangement of Ipsilateral Knee. C. J. Sutro.—p. 513.
Present Concepts of Benign Breast Disease. I. T. Nathanson.—p. 516.
Carcinoma of Pancreas, with Metastases to Regional Lymph Nodes, Liver, Lungs and Pleura. Thrombosis of Portal Vein and Right Hepatic Artery. Massive Infarction of Liver.—p. 521.
Cirsoid Aneurysm of Left Gastric Artery, with Secondary Peptic Erosion.—p. 524.

235:533-570 (Oct. 10) 1946

Scarlet Fever: Epidemiologic and Bacteriologic Study of Cases Occurring in Small Community. A. D. Rubenstein and G. E. Foley.—p. 533.
Acute Salpingitis Due to Friedländer's Bacillus: Report of Case. T. W. Botsford and T. D. Kinney.—p. 539.
Cause, Relief and Prevention of Headaches Arising from Contact with Dynamite. A. M. Schwartz.—p. 541.
Terminal Ileitis with Obstruction and Abscess Complicating Pregnancy. W. W. Babson.—p. 544.
Present Concepts of Benign Breast Disease. I. T. Nathanson.—p. 548.
Acute Rheumatic Myocarditis.—p. 554.
Hepatoma, with Portal Vein Invasion and Thrombosis; Cirrhosis of Liver, Alcoholic Type; Esophageal Varices, with Massive Hemorrhage. —p. 557.

235:571-604 (Oct. 17) 1946

Enteric Infections and Their Sequelae. R. A. Lewis.—p. 571.
*Surgical Treatment of Ascites. R. C. Crosby and E. A. Cooney.—p. 581.
Tuberculosis of Genitourinary Tract Among Soldiers in World War II. R. Chute.—p. 586.
Acute Pulmonary Edema, with Special Reference to Experimental Studies. P. H. Henneman.—p. 590.
Embolism of Superior Mesenteric Artery.—p. 596.
Papillary Carcinoma (Grade II A), Involving Upper Half of Bifid Pelvis. —p. 599.

Surgical Treatment of Ascites.—In treating ascites Crosby and Cooney insert a glass button into the lower rectus sheath so that ascitic fluid may drain from the peritoneal cavity into the subcutaneous tissues and be absorbed as edema fluid. Five cases of Laënnec's cirrhosis of the liver and 1 of chronic constrictive pericarditis are reported, in all of which the ascites was treated by the insertion of the button. The rationale for the use of the button is to obviate repeated abdominal paracenteses. Its main advantage over previous surgical measures is its simplicity of application. An additional value is that it returns to the patient his own ascitic fluid together with its protein content as a constant, slow clysis as long as the fluid is formed.

235:605-636 (Oct. 24) 1946

*Subacute Bacterial Endocarditis: Report of 2 Cases Successfully Treated witht Penicillin. B. F. Massell and T. D. Jones.—p. 605.
*Hemostasis by Thrombin and Fibrin Foam in Suprapubic Prostatectomy: Analysis of 40 Cases. W. C. Quinby.—p. 609.
Treatment of Mental Illness at Home by Small Doses of Insulin: Appraisal of Results in 12 Cases. N. Cohen.—p. 612.
Significance of Mediastinal Emphysema: 2 Cases. W. P. Vanderlaan and G. Maresh.—p. 617.
Acute Pulmonary Edema, with Special Reference to Experimental Studies. P. H. Henneman.—p. 619.
Strangulation of Bowel by Adhesive Band.—p. 628.
Ewing Tumor of Clavicle.—p. 630.

Penicillin in Subacute Bacterial Endocarditis.—Massell and Jones present the histories of 2 patients with subacute bacterial endocarditis who were cured by penicillin. The resistance to penicillin of the causative organism in 1 case was greater than that of any other successfully treated case reported in the medical literature. The correlation of the clinical picture with the penicillin sensitivity of the causative organism is of interest: 1 patient was extremely ill, and the causative organism was extremely sensitive to penicillin; the other was mildly ill, and the causative organism was relatively resistant to penicillin.

Thrombin and Fibrin Foam in Suprapubic Prostatectomy.—Quinby dissolves thrombin powder in about 10 cc. of isotonic solution of sodium chloride and immerses into it pieces of foam about 1.5 to 2 cm. square. These pieces are then placed in the cavity of the prostate after suprapubic prostatectomy. This method of hemostasis was employed in 40 cases, and it

is noteworthy that secondary bleeding occurred in none of the cases. Lavage of the bladder could be abandoned early, and the wound was healed and dry and voluntary urination had been resumed, on the average, eleven and a half days after operation.

North Carolina Medical Journal, Winston-Salem

7:533-584 (Oct.) 1946

Some Aspects of Sex Endocrinology in General Practice. E. C. Hamblen.—p. 533.
*Increase in Diphtheria Incidence in 1945. C. P. Stevick.—p. 540.
The Rh Factor. L. DeCamp.—p. 544.
Rationale for Treatment of Angina Pectoris by Irradiation of Adrenal Glands. W. C. Fisher and R. L. McMillan.—p. 547.
Treatment of Angina Pectoris by Irradiation of Adrenal Glands: Clinical Experience. R. L. McMilland and J. P. Rousseau.—p. 550.
*Effect of Immunization on Epidemic Influenza. T. R. Broadbent and E. E. Menefee.—p. 553.
Exfoliative Dermatitis Caused by Sulfonamides and Its Reproduction by Simple Patch Testing. J. Farrington and B. P. Wolff.—p. 555.
Thumbnail Sketches of Eminent Physicians: Story of Yellow Fever. W. C. Gorgas.—p. 556.

Increase in Diphtheria.—A higher incidence of diphtheria in North Carolina than in the United States as a whole is ascribed by Stevick to the fact that North Carolina has an inadequately immunized population. The major defect in the North Carolina immunization program is that the number of infants receiving a complete primary immunization is inadequate and not that the immunizing agent is ineffective or that new and more virulent strains of the diphtheria organism have developed. It is suggested that immunization of all infants at 6 months of age, followed by the administration of booster doses of the immunizing agent at 1 and 5 years, would afford more adequate protection.

Effect of Immunization on Epidemic Influenza.—During an epidemic of influenza at Duke University 85 male students were vaccinated after the onset of the epidemic, while 1,956 other male students were not immunized. In the vaccinated group the incidence of influenza was 2.3 per cent, while in the control group the incidence was 8.6 per cent. Furthermore, some of the control group developed complications. Broadbent and Menefee conclude that vaccination affords protection against influenza, and they suggest that results might have been even better if immunization had been given somewhat earlier.

Northwest Medicine, Seattle

45:709-796 (Oct.) 1946

Management of Acute Intestinal Obstruction. K. C. Sawyer.—p. 735.
Anesthesia and Analgesia in Obstetrics. E. S. Taylor.—p. 740.
Continuous Spinal Anesthesia in Obstetrics. R. E. Gillett.—p. 743.
Caudal Analgesia for Obstetrics in Private Hospital. J. D. Kindschi.—p. 747.

45:799-884 (Nov.) 1946

Disability Evaluation. H. C. Hughes.—p. 827.
Chylous Cyst of Mesentery in 4 Year Old. T. J. Taylor.—p. 834.
Differential Diagnosis in Right Renal Disease. C. C. Goodhope.—p. 836.
Internal Perforation of Urachal Abscess. H. M. Blegen.—p. 838.
*Use of Curare in Abdominal Surgery. M. A. Howard.—p. 840.
*Cellophane Wrapping and Ligation of Patent Ductus Arteriosus. K. Poppe.—p. 842.
Early Decortication in Clotted Hemothorax and Empyema. H. B. Kellogg.—p. 843.
Benadryl: B-Dimethylaminoethyl Benzhydryl Ether Hydrochloride. J. E. Stroh.—p. 846.
Pulmonary Tuberculosis and Other Thoracic Diseases Among Army Separatees. W. W. Lindahl.—p. 848.
*Delayed Allergic Reaction to Penicillin in Oil and Wax Treated with Procaine Intravenously. L. J. Rosellini and C. W. Van Rooy.—p. 849.

Curare in Abdominal Surgery.—Howard used curare in conjunction with ethylene, cyclopropane, ether and sodium pentothal in anesthetizing 208 patients who underwent abdominal operations such as appendectomy, colostomy, bile duct exploration, hemorrhoidectomy, herniaplasty and hysterectomy. From 1 to 7 cc. of the curare preparation intocostrin was administered in divided doses. Curare provided excellent relaxation without undue risk. There was no operative mortality.

Cellophane Wrapping and Ligation of Patent Ductus Arteriosus.—Poppe thinks that cellophane wrapping and ligation is the simplest and safest method of dealing with a patent ductus arteriosus. A physiologically reactive variety of cellophane such as polythene should be used in preference to an inert type. The optimal time for ligation appears to be immediately after the recovery from an acute episode after six or eight weeks of penicillin therapy, before the patient has another attack.

Delayed Allergic Reaction to Penicillin Treated with Procaine Intravenously.—Rosellini and Van Rooy report that a man aged 28 developed a generalized itching rash and arthralgia more than a week after he had been given several injections of penicillin in oil and wax for an infraorbital abscess. After conservative methods had failed to counteract the rash, 1 Gm. of procaine hydrochloride was dissolved in 500 cc. of isotonic solution of sodium chloride and was given intravenously over a period of two hours. Before the infusion was completed the patient felt better. The urticaria was rapidly disappearing. The joint symptoms were somewhat alleviated.

Ohio State Medical Journal, Columbus

42:993-1096 (Oct.) 1946

Management of Malaria. T. P. Sharkey.—p. 1025.
Etiologic Approach to Chronic Urticaria and Angioneurotic Edema. L. E. Lieder and L. L. Pennock.—p. 1035.
Cyclopropane Anesthesia: Evaluation of Ten Years of Experience. A. A. Brindley—p. 1043.
Use of Pessary as Adjunct to Early Rising in Puerperium. C. W. Pavey.—p. 1047.
Volvulus of Ileum with Intertwining Loops and Knot Formation. C. S. Becker.—p. 1050.

42:1097-1216 (Nov.) 1946

American Democracy and American Medicine. E. J. McCormick.—p. 1129.
Advances in Electrocoma Therapy of Psychoses. J. L. Fetterman.—p. 1133.
Coronary Heart Disease. A. B. Brower.—p. 1137.
Diagnosis of Nontraumatic Intracranial Lesions. W. J. Gardener.—p. 1144.
War Advances Anesthesia. K. C. McCarthy.—p. 1150.
Pharmacology and Therapeutic Aspects of Goiter Thiourea and Thiouracil. H. N. Cavanaugh and C. B. DeCourcy.—p. 1154.

Public Health Reports, Washington, D. C.

61:1397-1424 (Sept. 27) 1946

Typical Structures on Replicas of Apparently Intact Tooth Surfaces. D. B. Scott and R. W. G. Wyckoff.—p. 1397.
Chemoprophylaxis of Experimental Influenza Infections in Eggs. R. H. Green, A. F. Rasmussen Jr. and J. E. Smadel.—p. 1401.
Separation of Complement Fixing Agent from Suspensions of Yolk Sac of Chick Embryo Infected with Karp Strain of Tsutsugamushi Disease (Scrub Typhus). Ida A. Bengtson.—p. 1403.

61:1425-1468 (Oct. 4) 1946

Tuberculosis Control in Denmark. J. Holm.—p. 1426.
Tuberculosis Mortality in Major Cities: United States, 1944. Elizabeth H. Pitney and R. V. Kasius.—p. 1443.

61:1469-1500 (Oct. 11) 1946

Study of Rodent Ectoparasites in Mobile, Ala. L. C. Cole and Jean A. Koepke.—p. 1469.

61:1501-1528 (Oct. 18) 1946

Industrial "Control Chart" Applied to Study of Epidemics. W. H. Rich and M. C. Terry.—p. 1501.
Evaluation of Three Plague Vaccines Against Infection in Guinea Pigs Induced by Natural and Artificial Methods. N. E. Wayson, Margaret C. McMahon and F. M. Prince.—p. 1511.

Puerto Rico J. Pub. Health & Trop. Med., San Juan

22:1-136 (Sept.) 1946

*Brucellosis: Review of Its Clinical Manifestations, with Presentation of 12 Cases Occurring in Puerto Rico. F. Hernández Morales.—p. 3.
Hookworm Infestation in Small Town of Puerto Rico. J. Peterson, G. Arbona and Josefina Acosta.—p. 48.
Filarial Survey Among Young Puerto Ricans. Z. T. Bercovitz and H. Shwachman.—p. 66.
Filariasis in Puerto Rico: Note on Family Incidence. F. Hernández Morales and J. Oliver González.—p. 95.
Incidence of Filariasis at Insular Penitentiary for Men. F. Hernández Morales and G. Gonzáles Barrientos.—p. 99.
Roentgen Pathology of Duodenal Ulcer: Observations in Tropical Area. M. Guzman.—p. 106.

Brucellosis.—Hernández Morales reports 8 cases of acute and 4 of chronic brucellosis. The electric refrigerator probably plays a part in the rising incidence of brucellosis in Puerto Rico. Our grandfathers had to boil their milk before drinking it so as to prevent its souring and in this way unwittingly combated the disease. Today, milk can be easily preserved raw; moreover, raw milk is cheaper than pasteurized and is served

almost everywhere, especially in restaurants. It is also utilized in the making of cheese. No law forbids its use unpasteurized. Unless preventive measures are established, the disease will become widespread.

Southern Medical Journal, Birmingham, Ala.

39:847-920 (Nov.) 1946

*Vaginal Cell Examination as Routine in Diagnosis: Study of Vaginal and Cervical Cytology as Related to Abnormal Growths. J. E. Ayre. —p. 847.
Histopathology of Common Primary Swellings of Peripheral Lymph Nodes. H. A. Horn.—p. 853.
*Primary Tularemia Pneumonia Treated with Streptomycin: Report of 2 Cases. D. T. Smith and R. J. Atwell.—p. 858.
*Pharmacologic and Radiologic Study of Hemophilia. M. Ostro and D. I. Macht.—p. 860.
Examination of Back: Diagnostic Outline for Standardized Routine. E. D. McBride.—p. 867.
Amebiasis. R. A. Robinson.—p. 876.
Coexistent Hookworm and Tuberculosis. T. C. Black.—p. 881.
Chronic Infestation with Intestinal Parasites in Engineer Battalion with Particular Reference to Schistosoma Japonicum. W. B. Martin, J. G. Graziani, J. Collins and D. R. Lincicum.—p. 885.
Infections of Neck Following Tooth Extractions. V. D'Ingianni.—p. 889.
Thiouracil: Clinical Evaluation Following Two and One-Half Years' Experience. D. L. Sexton.—p. 891.
Diverticula of Digestive Tract: Review of Literature, with Observations Based on Survey of 1,000 Consecutive Office Cases. W. M. Ballinger. —p. 897.
*Appendicitis: Clinicopathologic Study. W. R. Moses.—p. 902.
Hydrogen Ion Concentration of Senile Vaginal Mucosa Before and After Estrogenic Therapy. K. J. Karnaky.—p. 906.
Incidence of Pulmonary Consolidations in Mild Asthmatic. D. O. Wright, E. M. Gold and G. Jennings.—p. 908.

Vaginal Cell Examination.—Ayre reviews observations on 2,320 gynecologic cases in which a cytologic study for malignant growths was made. Genital cancer has been diagnosed by cytology and confirmed by biopsy in 202 cases. The centrifuge technic and the glycerin method for mailing cytologic specimens are briefly described. A group of preclinical, asymptomatic cases has been detected by routine cytologic tests, and a new cell complex has been described in cases showing a linkage of abnormally high cornification (estrogen) with a measurable thiamine deficiency. These cases have been grouped as precancerous.

Streptomycin in Primary Tularemic Pneumonia.—Atwell and Smith present the histories of 2 Negro boys aged 13 and 17. The two lived in the same room and were exposed to dog ticks and to rabbits brought into the house by their dogs. The date of the exposure could not be determined and no local dermal lesion could be found, but the serums agglutinated tularense antigen. The first patient was much more seriously ill than the second and almost moribund at the time streptomycin therapy was started. Both patients seemed to improve clinically after about two days of streptomycin. In the case of the massive pleural effusion, it seemed that the intrapleural streptomycin was very efficacious in eliminating the organism and in stopping the formation of fluid. The doses of streptomycin were rather large, but it was felt that the highly fatal primary pneumonic form of the disease would require more intensive treatment than the milder ulceroglandular type of tularemia.

Radiologic Study of Hemophilia.—Ostro and Macht describe investigations which revealed that irradiation with x-rays noticeably shortens the coagulation time of blood specimens from animals and human beings in vitro. Two hemophilic patients treated with x-rays over the splenic region showed considerable shortening of coagulation time for some time afterward. The authors hope that this preliminary report will stimulate further investigation.

Appendicitis.—Moses thinks that appendicitis in its usual form is initiated by obstruction of the lumen of the organ. If this obstruction is not relieved, either spontaneously or by surgical intervention, there follows venous obstruction with outpouring of an edematous exudate. It is this phase which is usually seen when the viscus is described as "red hot." During this stage the wall comes to act as a permeable membrane to the luminal bacteria with the possibility of a "localized peritonitis" in the absence of demonstrable perforation. If this process of venous obstruction is allowed to persist, arterial occlusion by spasm, extrinsic pressure on the vessel or thrombosis will supervene, with resultant perforation or gangrene, the extent of the necrosis depending on the size of the occluded vessel. The role of bacteria appears to be solely that of a secondary invader.

Surgery, Gynecology and Obstetrics, Chicago

83:417-560 (Oct.) 1946

*Subtotal Esophagectomy with High Intrathoracic Esophagogastric Anastomosis in Treatment of Extensive Cicatricial Obliterans of Esophagus. R. H. Sweet.—p. 417.
Suppurative Cholangitis Complicating Sidetracking Operations of Biliary Tract. J. Zaslow and V. S. Counseller.—p. 428.
Surgical Significance of Aortic Arch Anomalies. R. E. Gross and P. F. Ware.—p. 435.
Thrombophlebitis of Deep Veins in Thromboangiitis Obliterans. J. W. Kahn.—p. 449.
Relative Surgical Curability of Certain Gross Types of Gastric Carcinoma. R. Schindler.—p. 453.
Management of Plastic Maxillofacial Wounds in Evacuation Hospital. C. H. Leech, B. C. Drum and H. F. Osterhagen.—p. 462.
Transverse Presentation. J. T. Cole and F. Delany.—p. 473.
*Gastric Cancer: Laparotomy, Resectability and Mortality. S. N. Maimon and W. L. Palmer.—p. 480.
*Bilateral and Multiple Ruptured Disks as One Cause of Persistent Symptoms Following Operation for Herniated Disk. F. A. Echlin, B. Selverstone and W. E. Scribner.—p. 485.
Metastatic Hypernephroma of Thyroid Gland. R. R. Linton, J. D. Barney, H. D. Moorman and J. Lerman.—p. 493.
Malformation of Anus and Rectum. M. S. Rosenblatt and A. May. —p. 499.
Management of Osteomyelitis Secondary to War Wounds. K. A. Fischer.—p. 507.
Surgical Treatment of Gangrene in Trench Foot. H. B. Shumacker Jr. —p. 513.
Study of Absorption Characteristics of Surgical Catgut. G. Haugaard, L. A. Thoennes and M. J. Hall.—p. 521.
Effect of Anticoagulants on Postpartum Bleeding. A. C. Barnes and H. K. Ervin.—p. 528.
*Talc Granuloma. A. L. Lichtman, J. R. McDonald, C. F. Dixon and F. C. Mann.—p. 531.

Subtotal Esophagectomy in Cicatricial Obliteration.—Three patients with cicatricial obliteration of a large portion of the esophagus as a result of chemical burns were treated by radical esophagectomy. In 2 of these the upper limit of the lesion was low enough to make it possible to perform the anastomosis a short distance below the arch of the aorta. In the third the proximal extent of the obstructed area was so high that the anastomosis when completed lay behind the level of the jugular notch. In this case a subtotal esophagectomy was performed. All 3 patients made a complete recovery. Sweet concludes that in cases of intractable stricture of the esophagus resulting from chemical burns an esophagectomy followed by a high intrathoracic esophagogastric anastomosis is superior to any form of external esophagoplasty.

Gastric Cancer: Resectability and Mortality.—Maimon and Palmer analyze the present status of the surgical treatment of gastric cancer with respect to exploratory laparotomy, resectability and postoperative mortality on the basis of 576 patients with gastric carcinoma who were examined over a seventeen year period at the University of Chicago. Laparotomy was carried out on 389, or 83.5 per cent, of the 466 patients who followed the advice given. The remaining 16.5 per cent were inoperable. The resectability rate in the 389 submitted to exploration was 52.1 per cent. The resection survival rate in the 203 patients undergoing resection was 73.7 per cent. The mortality in unselected cases of partial resection was 22.6 per cent before 1940 and 16.3 per cent after 1940. The percentage of patients considered operable is increasing; the resectability rates are becoming higher and the postoperative mortalities are decreasing in spite of the greater incidence of complicated and extensive operations. Nevertheless the outlook for prolonged survival continues to be limited.

Bilateral and Multiple Ruptured Disks.—Echlin and his associates review observations on 60 patients who were operated on for suspected herniation of a lumbar disk. One patient was found at operation to have three ruptured disks, 6 patients two herniated disks and 3 patients a bilateral herniation of an intervertebral disk requiring bilateral removal. In 2 other patients, from each of whom a ruptured disk had been removed elsewhere at the fifth lumbar level, a second herniated disk was found on the same side as the original exploration but in both cases at the interspace above. From another patient who had

had a negative exploration elsewhere at the third lumbar level the authors removed two herniated disks. In still another instance a herniated disk was extirpated at the fifth lumbar level on the left in a patient from whom a herniated disk had been removed elsewhere from the same interspace on the opposite side. Thus 6⅔ per cent of the patients had bilateral and 16⅔ per cent had multiple herniated disks.

Talc Granuloma.—Lichtman and his associates state that the tissue damage caused occasionally by talc is a heavy price to pay for the preservation of a pair of rubber gloves. Granulomatous lesions of the peritoneum, draining sinuses, scar nodules and malfunctioning intestinal stomas were found at secondary operations. Polarized light microscopy was of great value in identifying talc crystals and in studying the pathogenesis of talc granuloma. The authors think that talc granulomas would be recognized more frequently if there were greater use of polarized light microscopy.

83:561-704 (Nov.) 1946

*Nutrition in Pregnancy: Effects of Dietary Deficiency in Pregnancy and Detection and Treatment of Nutritional Deficiency Diseases. C. F. Vilter, D. Morgan and T. D. Spies.—p. 561.
*Gastric Carcinoma: Incidence and Diagnostic Procedures. S. N. Maimon and W. L. Palmer.—p. 572.
Continuity of Fasciae Lining Abdomen, Pelvis and Spermatic Cord. C. E. Tobin, J. A. Benjamin and J. C. Wells.—p. 575.
*Transurethral Resection in Surgical Management of Cord Bladder. J. L. Emmett and J. H. Dunn.—p. 597.
Appendicitis in Cleveland: Final Report. H. W. Green and R. M. Watkins.—p. 613.
Arteriovenous Fistulas of Cervical Portion of Vertebral Vessels. H. B. Shumacker Jr.—p. 625.
*Tendon Transplantation in Hand. H. May.—p. 631.
Further Experiences with Paularyngectomy for Advanced Carcinoma of Larynx. A. Brunschwig and J. R. Lindsay.—p. 639.
Operative Technic of Thoracolumbar Sympathectomy. J. W. Hinton and J. W. Lord Jr.—p. 643.
Clinical Evaluation of Sotradecol, a Sodium Alkyl Sulfate Solution, in Injection Therapy of Varicose Veins. W. M. Cooper.—p. 647.
Therapy for Soft Tissue Sarcomas: Experimental Study: M. E. Maun, F. C. Jewell and W. F. Dunning.—p. 653.
Transthoracic Operations for Neoplasms of Esophagus and Stomach. G. W. Nagel and J. F. Menke.—p. 657.
Vascular Injuries in War. B. Bradford Jr. and M. J. Moore.—p. 667.

Dietary Deficiency in Pregnancy.—Vilter and his associates present cases which illustrate dietary deficiency in pregnancy. The cases show neuritis of thiamine deficiency in a woman aged 27, pellagrous glossitis in a mother aged 35 in the last trimester of her seventh pregnancy and riboflavin deficiency symptoms in the mother of 8 children during a period of lactation. The principles of treatment for nutritional disease occurring during pregnancy do not differ from those generally prescribed in nutritional deficiencies. They include a high caloric diet including from 120 to 150 Gm. of protein and adequate minerals and vitamins as well as synthetic vitamins directed at the more prominent symptoms and finally a natural source of vitamin B complex such as brewers' yeast, crude liver extract or wheat germ.

Gastric Carcinoma: Incidence and Diagnosis.—On the basis of studies on more than 500 cases of gastric cancer observed over a seventeen year period Maimon and Palmer conclude that the incidence of gastric cancer rises sharply with advancing age, approximately three fourths of the cases occurring after 50. Thus gastric cancer will increase in incidence as the average age of the population rises. Gastroscopy yielded the correct diagnosis in 84.6 per cent of the cases in which it was utilized. X-ray examination provided the correct diagnosis in 91.8 per cent of the cases so examined. "Dyspeptic" symptoms appearing in patients of the "cancer age" warrant prompt roentgenologic and gastroscopic study.

Transurethral Resection in Surgical Management of Cord Bladder.—Emmett and Dunn say that in 1944 one of them (Emmett) reported his experience in 20 cases of true cord bladder in which transurethral resection had been carried out. During the two year period from 1944 to 1946 transurethral resection was carried out at the Mayo Clinic on 45 patients who had neurogenic bladder resulting from injury or disease of the spinal cord. Thirty of these patients were suffering from a transverse lesion of the spinal cord, whereas the neurologic disease of the remaining 15 consisted of multiple sclerosis (7 patients), combined sclerosis (4 patients) and miscellaneous lesions of the spinal cord (4 patients). The authors present a number of illustrative case reports. They conclude that cord bladder no longer is a hopeless situation. Satisfactory vesical function can be restored by mechanical adjustment of the vesical neck and by teaching the patient to use unaffected muscles to aid him to void. Mechanical adjustment of the vesical neck is brought about by transurethral resection.

Tendon Transplantation in the Hand.—May describes and illustrates methods of tendon grafting in various regions of the hand. In stressing the importance of postoperative care he says that it is a common belief that motion, if started early, will prevent the adhesion of tendons, yet the opposite seems to be the case. Early motion favors adhesions not only because of irritation of the surrounding tissue but also because the vascularization of the tendon is disturbed. The author prefers the molded plaster cast splint. The hand is placed in such a position that the suture line is under a minimum of tension. After two and one-half weeks splint and dressings are taken off temporarily and the sutures removed. The forearm and hand are placed from now on daily in a warm saline bath, and active motion exercises are encouraged. The splint is reapplied after the bath. Three weeks after the operation the splint is discarded, and local heat, massage and passive exercises are added to the active exercises.

United States Naval Med. Bulletin, Washington, D. C.

46:1639-1782 (Nov.) 1946

Wartime Log of United States Navy Hospital Ship to 30 June 1943: Part I. M. J. Aston and R. A. Kern.—p. 1639.
*Use of Tantalum in Tendon Reconstruction of Hand. R. C. Pearlman.—p. 1647.
Redundant Duodenum. Radiographic Study. I. H. Slater and A. Lautkin.—p. 1651.
Proctology in U. S. Naval Hospital: Analytic Review of Six Month Period. C. E. Pope.—p. 1658.
*Evaluation of Therapeutic Agents in Plague: Review of Literature. R. F. Platzer.—p. 1674.
Alcohol as Factor in Naval Delinquencies. A. C. Cornsweet and B. Locke.—p. 1690.
Treatment for Otitis Externa in the Tropics. G. O. Dean.—p. 1696.
Colloid Mucostatic Impression Technic for Full Lower Dentures. W. J. Cunningham and M. R. Pope.—p. 1698.
Endogenous versus Exogenous Origin of Reinfection Type Pulmonary Tuberculosis: Case Report. W. H. Harris Jr.—p. 1702.
Capillary Fragility in Rheumatic Fever. H. Montgomery.—p. 1708.
*Penicillin Prophylaxis Against Acute Otitis Media in Scarlet Fever. J. A. Weiss and P. J. Manheims.—p. 1711.
Influence of Combat on Incidence of Intestinal Parasites. H. K. Russell, E. W. Eisenhower and D. J. Roose.—p. 1716.
*Penicillin in Treatment of Louse Borne Relapsing Fever. H. S. Ingraham and R. G. Lapenta.—p. 1719.
Diagnosis and Surgical Management of Thoracoabdominal Wounds Aboard an Assault Transport. J. N. O'Neill.—p. 1724.

Tantalum in Tendon Reconstruction.—So many excellent jobs of tendon reconstruction have been spoiled by adhesions that Pearlman decided to use tantalum foil 0.00025 inch in thickness as an interpositional substance. This has often made it unnecessary to resect a tendon that is scarred and adherent. A tendon with raw surfaces was simply encased within tantalum foil and the foil held in place with catgut ligatures. The tantalum-wrapped tendon was then dropped back into its normal channel. The tantalum foil did not need to be removed. At the end of four to six weeks the tendon was "free" in its channel; the foil was found fragmented and adherent to adjacent tissues. The tendon itself was coated with a glistening layer of cells.

Therapeutic Agents in Plague.—Platzer states that sulfadiazine is the drug of choice in the treatment of plague. It must be given early in doses of 12 to 30 Gm. on the first day and smaller doses for twelve days after the temperature is normal. The best results have been obtained when the combined treatment with antiplague serum and sulfadiazine has been used. Antiplague serum and sulfadiazine are of value prophylactically in cases of exposure to plague.

Penicillin to Prevent Acute Otitis Media in Scarlet Fever.—Weiss and Manheims review observations of 239 cases of scarlet fever. They found penicillin greatly superior to sulfadiazine not only in the prevention of acute otitis media but also in the treatment of active otitic suppuration. Administration of 20,000 units every three hours for five to seven days is recommended.

Penicillin in Louse Borne Relapsing Fever.—According to Ingraham and Lapenta, louse borne relapsing fever appeared in Egypt after an absence of over twenty years. Penicillin was tried in a series of 52 cases, and 53 served as controls. The disease was relatively mild, with a fatality rate of 5 per cent in the untreated cases. The initial bout of fever lasted seven days on the average, with termination by crisis. The remission averaged eight days in length, followed by an abrupt recurrence in which the mean duration of symptoms was four days. A second relapse was unusual in this epidemic. Penicillin was given intramuscularly every three hours in 25,000 unit doses up to a total of 1,000,000 units. Cure was obtained in all 52 cases and no relapse followed, whereas in the controls relapse occurred in 87 per cent of the cases.

Urologic & Cutaneous Review, West Palm Beach, Fla.

50:517-580 (Sept.) 1946

Urinary Extravasation. D. E. Beard.—p. 517.
Lymphogranuloma Venereum: Report of Case in Child. H. L. Weinstock and S. Keesal.—p. 520.
Ectopic Pelvic Kidney: Report of Case with Huge Hydronephrosis. D. P. Slaughter and N. J. Heckel.—p. 522.
Unusual Renal Obstruction Following Trauma. O. S. Culp.—p. 524.
Thromboangiitis, Phlebitis and Lymphangitis of Spermatic Cord in Relation to Lymphogranuloma Venereum. W. E. Coutts and R. Vargas Zalazar.—p. 526.
Male Infertility. R. J. Douglas.—p. 529.
Malignancies of Urinary Tract: Five Year Survey, with Report of Unusual Case. R. P. Beatty.—p. 531.
What Part Does Posture Play in Ischemia and Stasis of Pelvic Organs? Description of Fatigue by Tests and Report of Cases. F. H. Redewill.—p. 535.
Treatment of Dermatophytid. A. A. Holbrook.—p. 542.
Epidermolysis Bullosa Hereditaria. M. M. Robinson.—p. 545.

Yale Journal of Biology and Medicine, New Haven

19:1-140 (Oct.) 1946

*Tubercle Bacillus and Fundamental Chemotherapeutic and Antibiotic Action. H. J. Corper and M. L. Cohn.—p. 1.
*Oxygen Pressure Gradient Between Maternal and Fetal Blood in Pregnant Sheep. D. H. Barron.—p. 23.
Hemagglutination Induced by Viruses. B. A. Briody Jr.—p. 29.
*Probable Role of Histamine in Some Emotionally Precipitated Allergic Conditions. W. T. Brown.—p. 63.
Electrophoresis in Medicine. K. G. Stern and Miriam Reiner.—p. 67.
Use of Micro-Organisms for Therapeutic Purposes. H. W. Florey.—p. 101.
Early Surgical Operations. H. W. Jones.—p. 119.
Familial Periodic Paralysis: Report of Case Showing No Changes in Serum Potassium Level, with Description of Electroencephalographic Findings. C. W. Watson.—p. 127.

The Tubercle Bacillus and Chemotherapeutic and Antibiotic Action.—Corper and Cohn say that streptomycin administered in proper dosage is capable of retarding the growth of human tubercle bacilli both in vitro and in vivo. However, the concentration of streptomycin required to retard the growth of tubercle bacilli in vitro in good nutrient medium can be attained in vivo for only a brief period. Streptomycin is not tuberculocidal but produces its effects in vivo primarily as a retardant of the growth of tubercle bacilli when they are actively developing or reproducing. In clinical tuberculosis in man, the bacilli appear to reproduce and develop only at irregular periods undeterminable by clinical means and over long periods of time, and this reduces the applicability of a retardant without tuberculocidal action for use in human tuberculosis.

Oxygen Pressure Gradient Between Maternal and Fetal Blood.—Oxygen pressures were determined on sheep in the fetal umbilical artery, umbilical vein, uterine artery and uterine vein in the latter half of the gestation period. It was found that the pressure gradient favors the movement of oxygen from the maternal to the fetal blood.

Histamine in Allergic Conditions.—A man aged 34, who had a history of many allergic sensitivities (e. g. strawberries, tomatoes) presented the same clinical manifestations—generalized urticaria, rhinitis, sneezing, conjunctival hyperemia with profuse lacrimation and stomach discomfort with indigestion, burning, belching and nausea—after emotional excesses or contact with specific allergens. Brown thinks this case suggests that histamine plays a role in emotionally precipitated conditions that resemble allergies. Benadryl, which exerts an antihistamine action, was prescribed and it relieved the emotionally precipitated urticaria.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Brain, London

69:73-156 (June) 1946

Occlusion of Basilar Artery—Clinical and Pathological Study. C. S. Kubik and R. D. Adams.—p. 73.
Anosognosia and Disorders of Body Scheme. P. H. Sandifer.—p. 122.
Coughing and Unconsciousness: So-Called Laryngeal Epilepsy. A. F. Rook.—p. 138.
Effect of Rupture of Perineurium on Contained Nerve Fibers. S. Sunderland.—p. 149.

British Journal of Surgery, Bristol

34:1-108 (July) 1946

Hazards of Parachuting. P. Essex-Lopresti.—p. 1.
Inguinal Hernia: Unpredictable Result. W. J. M. Brandon.—p. 13.
*Surgical Treatment of Carcinoma of Esophagus: with Special Reference to New Operation for Growths of Middle Third. I. Lewis.—p. 18.
Chronic Osteomyelitis, The Sequel to Gunshot Wound. G. Perkins.—p. 31.
Study of Fate of Nerve Homografts in Man. R. Barnes, P. Bacsich, G. M. Wyburn and A. S. Kerr.—p. 34.
Analysis of Series of 454 Inguinal Hernias with Special Reference to Morbidity and Recurrence After Whole Skin Graft Method. G. B. Mair.—p. 42.
Case of Albright's Syndrome (Osteitis Fibrosa Disseminata). R. C. Murray, H. J. R. Kirkpatrick and E. Forrai.—p. 48.
Saccular Diverticulosis of Jejunum Due to Reticulum Cell Sarcoma. A. G. Williams and J. H. Fodden.—p. 57.
Further Review of Interinnomino-Abdominal Operation, Based on 21 Personal Cases. G. Gordon-Taylor and D. H. Patey.—p. 61.
Discussion on Treatment of Injuries to Hand. F. T. Moore.—p. 70.
Dislocation of Inferior Radio-Ulnar Joint. J. F. Curr and W. A. Coe.—p. 74.
Case of Acute Anaerobic Streptococcal Infection of Neck of Dental Origin. C. G. Boothroyd and C. Macleod.—p. 78.
Derangement of Midgut Rotation Producing Volvulus: Report of 2 Cases. C. E. P. Mardby.—p. 80.
Resection of Head of Pancreas. C. A. Pannett.—p. 84.
*Brodie's Disease of Breast. D. Aiken.—p. 87.

Carcinoma of Esophagus.—Lewis reports 7 cases of esophagectomy with 5 recoveries. He describes a new operation of resection with immediate anastomosis for cancer in the middle third of the esophagus. After mobilization of the stomach by laparotomy, a right transpleural esophagectomy is performed, the stomach being brought up through the dilated hiatus, fixed at any required level in the right pleura, and an end to side esophagogastrostomy performed.

Brodie's Disease of Breast.—Aiken reports a case of Brodie's tumor in a woman aged 68. The tumor was removed, and there was no recurrence. The author stresses that the term "Brodie's tumor" should be reserved for large, excessively cellular and long-neglected fibroadenomas. The history of a preexisting breast tumor of many years' duration which at first grows slowly or not at all and finally in the late middle years increases rapidly in size is the outstanding feature of Brodie's tumor. The skin overlying the tumor is mobile, and the lymph nodes are not usually involved. Enlargement may be so great that ulceration of the skin occurs from pressure necrosis, and the foul, fungating mass suggests a carcinoma. Sometimes the correct diagnosis of an innocent large tumor is impossible until the breast is removed. One striking clinical feature is the excellent general condition of the patient.

Edinburgh Medical Journal

53:465-528 (Sept.) 1946

*Sarcoidosis—A Manifestation of Tuberculosis. C. Cameron and E. K. Dawson.—p. 465.
Observations on Functional Heart Disease. I. G. W. Hill.—p. 485.
Ear-Pit (Congenital Aural and Pre-Auricular Fistula). I. Aird.—p. 498.
Tuberculosis in Sutherland with Special Reference to Surgical Tuberculosis. B. S. Simpson.—p. 508.

Sarcoidosis and Tuberculosis.—Cameron and Dawson report a case of pulmonary tuberculosis with pathologic changes in other tissues, which conformed with the accepted clinical and histologic features of sarcoidosis. The case is noteworthy because tubercle bacilli were recovered by culture in a sarcoidosis patient, for one of the salient characteristics of sarcoidosis is the difficulty with which Mycobacterium tuberculosis or any other criteria of the infection can be demonstrated. The history of the patient was a long one, from the initial disturbance at the

age of 5 to her death at the age of 19. Signs and symptoms varied during this long period. Some lesions, such as the iridocyclitis and splenic enlargement, improved and disappeared; others, like the joint disorder, the kidney lesion and the slight, irregular, varying temperature, remained more or less constant.

Glasgow Medical Journal

27:281-312 (Oct.) 1946

Determination of Total 17-Ketosteroids in Urine: Simplification of Method for Routine Use in Hospital Biochemical Laboratory. S. L. Tompsett and E. G. Oastler.—p. 281.
*Intussusception of Appendix. D. C. Miln.—p. 297.
Multiple Carcinoid Tumors of Bowel: Report of Case. A. Lyall.—p. 300.

Intussusception of Appendix.—Miln reports the case of a man aged 38 who in October 1945 had an attack of dysentery characterized by gastroenteritis, and severe griping abdominal pain. He was treated with sulfaguanidine, and the condition subsided, though he still complained of some ache in the right side of the abdomen which was worse during defecation. Palpation disclosed a tender mass in the right iliac fossa. Surgical intervention revealed an intussusception of the appendix into the cecum and partly into itself. The appendix was removed together with a small cuff of cecum.

Medical Journal of Australia, Sydney

2:433-468 (Sept. 28) 1946

*Costen's Syndrome: Hitherto Unrecognized Cause of Vague Head Pain. J. C. R. Bell.—p. 433.
Generalized Lymphatic Carcinomatosis (Cancerous Lymphagitis) of Lungs, with Special Reference to Miliary Carcinomatosis and Syndrome of "Granulie Froide." C. G. Lambie and J. Collier.—p. 439.
Klinefelter-Reifenstein-Albright Syndrome. H. F. Bettinger and B. Robinson.—p. 446.
Toxoplasmic Encephalomyelitis, with Report of 2 Cases. E. G. Robertson.—p. 449.

Costen's Syndrome and Head Pain.—Bell points out that Costen's syndrome is a hitherto unrecognized cause of vague head pain, which many patients have endeavored to describe with but little success. The symptoms are often bizarre. They usually arise because the mandibular condyle does not have a normal position in the articular portion of the mandibular fossa (glenoid fossa) throughout the various excursions of the mandible, these latter movements being controlled by the position of the teeth. The symptoms include dull pain within and about the ears; a "low buzz" type of tinnitus; a stuffy sensation in the ears; catarrhal deafness and dizzy spells which are relieved by inflation of the eustachian tubes; tenderness to palpation of the temporomandibular joints; sinus headache after sinus or ocular involvement has been found nonexistent; neuralgia; noisy, painful and either limited or excessive movement of temporomandibular articulation; burning or prickling sensation of tongue, throat and side of nose, and dryness of the mouth. Examination of the mouth and facial characteristics will generally more than hint at the loss of vertical dimension. Costen's syndrome is treated by increasing the maxillomandibular vertical dimension.

Thorax, London

1:143-210 (Sept.) 1946

Spreading Suppurative Pneumonitis. T. H. Sellors, L. G. Blair, L. E. Houghton and others.—p. 146.
Pulmonary Edema: Physiologic Considerations. I. De Burgh Daly.—p. 182.
*Effect of Asbestos, and of Asbestos and Aluminum, on Lungs of Rabbits. E. J. King, J. W. Clegg and V. M. Rae.—p. 188.
Bronchiectasis and Atelectasis: Temporary and Permanent Changes. F. P. L. Lander.—p. 198.

Effect of Asbestos on Lungs of Rabbits.—The purpose of the experiments described by King and his associates was to test whether short fiber asbestos is less damaging in the lungs of the rabbit than is long fiber asbestos and whether metallic aluminum will suppress any toxic effect produced by fiber asbestos. Four groups of animals were tested. All groups showed a foreign body reaction in the lungs. In animals in the long fiber experiments there developed a nodular reticulinosis comparable with the experimental silicotic nodule. In animals in the short fiber experiment there developed a diffuse interstitial reticulinosis. The addition of aluminum did not afford any benefit in any group.

Cadernos Científicos, Lisbon

1:99-240 (May) 1946. **Partial Index**

*Intradural Lipoma of Cauda Equina. D. Furtado and Vasconcellos Marques.—p. 127.

Lipoma of Cauda Equina.—The lipoma observed by Furtado and Vasconcellos Marques in a woman of 56 is the eighth to be reported in the literature. The differential diagnosis from other intradural tumors is made by the history of slow evolution of the tumor, rheumatic-like pain in the legs, lack of radicular pain and progressive loss of walking in the absence of paralysis. There may or may not be blockage of the spinal canal. Treatment is early surgical removal in order to prevent compression of the spinal cord. Pure intradural lipoma is congenital. It is benign. Differentiation from fibrolipoma or liposarcoma is made only by microscopic study of the tumor.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

90:1023-1062 (Aug. 24) 1946. **Partial Index**

Spirochetal Infections of Air Passages. L. Koster.—p. 1030.
*Primary Carcinomas of Neck (Branchiogenic Carcinomas). J. Wieberdink.—p. 1034.
Treatment of Hyperthyroidism with Thiouracil. T. F. Bloem.—p. 1039.
Endemic Leprosy. P. H. J. Lampe.—p. 1043.

Primary Carcinomas of Neck.—Wieberdink reports observations on 40 patients with branchiogenic carcinoma who were observed in the course of thirty years at the Antoni van Leeuwenhoek Hospital and compares them with 80 cases reviewed by Oliver in 1935. There were 34 men and 6 women, a sex ratio of 6:1, whereas Oliver observed a sex ratio of 9:1. The average age in Wieberdink's 40 cases was 66 years, in Oliver's cases 55 years. As in Oliver's patients, so also in those reviewed by the author, the first symptom was usually a painless swelling. There was a predominance in both groups of localization on the right side. Surgery followed by x-ray treatment has given lasting results. The prognosis in operable cases is definitely better than is usually assumed.

Acta Medica Scandinavica, Stockholm

124:511-606 (July 20) 1946

Investigations of Epinephrine Concentration in Blood: I. Quantitative Chemical Method for Determination of Concentration of Epinephrine in Blood. M. Kobro.—p. 511.
Continued Investigations into Elimination of Thiamine in Urine. T. Geill and H. Lindholm.—p. 522.
Serologic Studies in Experimentally Produced Polyarthritis. P. Hedlund and G. Lofstrom.—p. 535.
Influence of Serum Cholesterol Concentration on Cholesterol Deposits Seen in Xanthomatosis. M. Faber.—p. 545.
*Electrocardiographic Findings in Patients with Peptic Ulcer. K. Ørning, C. Sommerfelt and W. Fredriksen.—p. 564.
Investigations on Physiopathology of Erythrocytes: II. Reticulocytosis and Liberation of Erythrocytes from Bone Marrow. A. Nizet.—p. 590.

Electrocardiographic Findings in Patients with Peptic Ulcer.—Ørning and his associates found in studies on 579 ulcer patients with a normal heart that vagotonia manifests itself by bradycardia, respiratory arrhythmia, prolonged PQ interval, and in 10 per cent of the cases by a characteristic electrocardiogram with high T waves in at least two leads. Bradycardia is the most frequent sign of vagotonia, occurring in about 50 per cent of the male and about 25 per cent of the female ulcer patients. Respiratory arrhythmia is seen in about 25 per cent of both sexes. A prolonged PQ interval was noted in about 6 per cent of the men and about 3 per cent of the women. High T waves are also seen especially in men, often accompanied by an elevated ST line. These changes are especially pronounced in the younger age groups and are rare in patients over 50. The auriculoventricular conduction time shows increase up to and including the group of 50 to 59 years. In ulcer patients with hemorrhage, myopathic abnormalities will be found in about 35 per cent. The cause of these alterations must be sought in a vasomotor reflex with consequent myocardial anoxemia. Atropine, owing to its parasympatheticolytic action, will cause the electrocardiographic changes evoked by the vagus to disappear. A prolonged PQ interval which does not become normal after administration of atropine must therefore be occasioned by factors other than vagotonia.

Book Notices

An Introduction to Essential Hypertension. By Richard F. Herndon, M.D., F.A.C.P. Fabrikoid. Price, $2.50. Pp. 88, with 7 illustrations. Charles C Thomas, 301-327, E. Lawrence Ave., Springfield, Ill., 1946.

Here is a concise, readable exposition of the known facts and latest theories on essential hypertension. This little book takes up in orderly fashion the normal regulation of blood pressure and the etiology and mechanism of hypertension, with its physiology, pathology, clinical aspects, prognosis, diagnosis and treatment. Nowhere else has the experimental work of Goldblatt, Page, Prinzmetal, Child, Lewis, Smith and a host of other careful investigators been so successfully yet briefly summarized. The pith of all these experimental data has been clearly and concisely stated and a reasonable theory of the etiology and mechanism of hypertension deduced. However, it is not definitely accepted by the author. The action of renin on preangiotonin to produce angiotonin (hypertension of Braun-Menendez) and destruction of the latter by angiotonase is briefly discussed. The controversial question of the role of renal ischemia in the production of hypertension is fairly stated. The author considers the etiology of essential hypertension still unknown but considers the disease as a "deep-seated, constitutional disorder woven into the very structure and personality of the individual and that it probably represents a composite of multiple factors."

The physiology of hypertension is briefly, probably too briefly, discussed. However, numerous references to pertinent literature are included, making it easily possible for the reader to extend his knowledge of this important aspect of hypertension. The author points out that arterial hypertension may be produced by three mechanisms: increased cardiac output, increased blood viscosity and increased peripheral resistance, but that in essential hypertension the first two are normal and that therefore the immediate cause of the elevated blood pressure must be increased peripheral resistance. He believes this is due to an inherent hypertonus of the arterioles, independent of the nervous system and organic changes in the vessel walls.

The pathology of hypertensive disease is treated simply and accurately, with emphasis on the cardiac and renal changes. It is the extent of the hypertensive lesions in the heart or kidneys which largely determines the clinical picture and the immediate prognosis.

The clinical aspects of the disease are tersely and accurately presented. Four color plates depict the funduscopic appearance in the four groups of the Wagener-Keith classification. The usual course of symptoms associated with so-called benign or essential hypertension is well outlined. The fulminating type, generally known as malignant hypertension, is rightly considered as differing only in the tempo of the disease and is correctly defined as those cases showing the characteristic lesion of papilledema.

According to the author, the prognosis depends on one minor and three major factors. He considers the height of the blood pressure a minor factor. The major factors are the extent of the arteriolar lesions, the degree of atherosclerosis and the cardiac status. The first can be estimated by the funduscopic examination and tests of renal function. The second is dependent more on the duration of the hypertension than on the height of the blood pressure. The third is determined by "the efficiency and sufficiency of the coronary circulation." Age and sex also influence the prognosis.

The diagnosis of hypertension is considered from both practical and theoretical standpoints. He classifies hypertension as essential, nephritic and symptomatic. Under essential he places benign and malignant hypertension. Nephritic is subdivided into parenchymal, vascular, perinephritic and ureteral. Symptomatic hypertension is considered to include physiologic, cerebral, cardiovascular and endocrine disturbances. The discussion of these various forms is brief but on the whole accurate.

The chapter on treatment is somewhat disappointing. One has been led to assume from the up-to-date material in the preceding chapters that the recently published results of surgical treatment would be as carefully analyzed, but such is not the case. The author states that "no treatment is yet known which has ever cured or arrested the progress of essential hypertension, although their temporary palliative value, especially in the early stages, cannot be questioned." He is apparently unaware of the results reported in the extensive postoperative studies published during the last few years. It has been definitely shown that splanchnicectomy does arrest the progress of the disease in many patients, and even more significant is the improvement, including alleviation of symptoms, maintained lowered blood pressure and improvement in cardiac and renal status shown in a high percentage of those operated on, even when the preoperative hypertensive changes were advanced. Although claims of cures have not been made by any surgeons, numerous cases have been carefully studied over postoperative periods up to twelve years with maintained normal blood pressures and restored cardiac and renal status. Contrary to the author's opinion, malignant hypertension is a distinct indication for splanchnicectomy, provided the cardiac and renal functions have not been irrevocably impaired. The other phases of treatment are well covered, although one may not agree that the nitrites are of any real value.

This little book, with the exception of treatment, fulfils its mission "as an introduction to hypertension" well. It really does more than this; it summarizes clearly and concisely the modern concept of the disease and in addition gives a well chosen bibliography. The latter should be of real value to any one interested enough to peruse further the literature on this highly important and still controversial disease. We recommend the work for general reading.

Modern Development of Chemotherapy. By E. Havinga, H. W. Julius, H. Veldstra and K. C. Winkler. Monographs on the Progress of Research in Holland During the War, No. 4. Paper. Price, $3.50. Pp. 175, with 31 illustrations. Elsevier Publishing Company, Inc., 215 Fourth Ave., New York 3, 1946.

This monograph is one in about twenty-four on the progress of research in the Netherlands during the war. Apparently the purpose of the series is to reveal the work undertaken by scientists in the Netherlands during the five years of German occupation. Such revelation is of course interesting to every one concerned with science. However, the monographs present more than historical interest; they contain much factual information, and the modern development of chemotherapy is no exception. For those who are interested in details, this monograph will be of value by making more complete their repository of data. The book is well written, is in English, is made up of good paper and contains a large number of illustrations and tables and extensive bibliographies at the end of each chapter. The contents include discussions on the mechanism of action of the sulfonamides and of para-aminobenzoic acid, divided into bacteriologic investigations, physicochemical investigations, chemical investigations and pharmacologic, immunologic and clinical investigations. There also is a brief discussion of a phase of mycotherapy concerned with Expansine, a derivative of Penicillium expansum. Unfortunately there is no index.

The Artificial Kidney. By Dr. W. J. Kolff, Internist of the Municipal Hospital "Engelenbergstichting," Kampen (Holland), with the cooperation of J. Van Noordwijk. Paper. Pp. 92, with illustrations. J. H. Kok N. V., Kampen, Holland, 1946.

This is a condensed English translation of the original Dutch by W. J. Kolff. The apparatus described as artificial kidney is essentially a vividialyzer. It is operated on the principle of dialysis and is proposed to be utilized for the removal of catabolic products from the blood of uremic patients. The earliest attempts to dialyze blood outside the body was made by Abel, Rowntree and Turner. After many endeavors the author, in cooperation with H. T. J. Berk, constructed an apparatus suitable for clinical use. A good dialyzer must be built on the principle of providing a spread of a small quantity of blood over a large surface; the blood must circulate in a closed system and the blood as well as the rinsing liquid must be maintained in continuous movement. The standard rinsing liquid used in their cases contains 0.6 per cent sodium chloride, 0.2 per cent sodium bicarbonate, 0.04 per cent potassium chloride and 1.5 to 3 per cent glucose. The concentration of the minerals potassium, sodium and chlorine and the alkali reserve is closely observed during dialysis. Kolff employed continuous dialysis in which the blood coming from the radial artery flowed only once

through the apparatus and was then returned by way of the radial vein. This was sufficient to remove almost all the urea and other retention products from the blood. The largest quantity of urea removed in one dialysis amounted to 260 Gm. Other retention products removed are residual nitrogen, creatinine, uric acid, indoxyl, xanthoproteine and several chemotherapeutic substances.

The book contains a minute description of this artificial kidney apparatus with a full set of drawings, so that any good instrument maker should be able to construct the apparatus. Accurate instructions are also given for cleaning and sterilizing the apparatus. We are told that the Dutch edition contains a detailed account of the use of the artificial kidney in the treatment of the first 15 patients. Although 14 of the patients have died, the author feels that this cannot be held against the apparatus. It appears that the chances of recovery for these patients were so slight that recovery could hardly be expected. The 1 patient who was cured, he admits, probably would have recovered without the help of the apparatus. However, he insists that definite clinical improvement occurred in patients who appeared in an utterly hopeless condition and that death appeared to be postponed for a considerable time in spite of almost complete anuria.

Synopsis of Pathology. By W. A. D. Anderson, M.A., M.D., F.A.C.P., Professor of Pathology and Bacteriology, Marquette University School of Medicine, Milwaukee, Wisconsin. Fabrikoid. Second edition. Price, $6. Pp. 741, with 342 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1946.

In this edition Anderson continues to present pathology in a concise and compact form. Much of the book has been revised and greater emphasis given to tropical diseases, blast injuries, conditions important in military medicine and the nonbacterial infectious diseases. A discussion of epidemic hepatitis is now included. Although already beautifully illustrated, 78 new illustrations have been added. The references have been brought up to date. While these changes greatly enhance the usefulness of the book for reference or reorientation, they fail to correct its one serious though understandable fault, the superficiality of the first three basic chapters concerning inflammation, repair, regeneration, retrogressive changes and disturbances of circulation. Expansion of these chapters, which would not necessarily increase the size of the book if the unnecessarily large size of many of the illustrations was reduced, would greatly aid beginning medical and dental students and teachers of pathology. In the next edition it is hoped that the author will refrain from using the word pathology incorrectly as the synonym for the terms lesions or pathologic changes.

Modern Drug Encyclopedia and Therapeutic Index. Edited by Alexander B. Gutman, Ph.D., M.D., F.A.C.P., Assistant Professor of Medicine, College of Physicians and Surgeons, Columbia University, New York. Third edition. Fabrikoid. Price, $10. Pp. 1,157. Yorke Publishing Company, Inc., 49 W. 45th St., New York 19, 1946.

This book has become widely known as a reference source for information on the identity of proprietary articles. The third edition, like the preceding two editions, contains for each listed product a statement of composition, the name of the manufacturer, claims for actions and uses, dosage and how it is supplied. As a source of such information this book has real usefulness, but as a therapeutic guide its usefulness is definitely limited because even though the author has apparently attempted to omit "unreasonable claims" there are described many preparations with claims more reminiscent of advertising circulars than of the decisions of a critical therapeutic committee. The table of contents includes a foreword, a glossary, a list of pharmaceuticals, of biologic products and of allergens, a therapeutic index, manufacturers' and distributors' index and a general index.

Sex, Marriage and Family. By Thurman B. Rice, A.M., M.D., Professor of Bacteriology and Public Health, Indiana University School of Medicine, Indianapolis. Cloth. Price, $2.50. Pp. 272. J. B. Lippincott Company, 227 S. Sixth St., Philadelphia 5, 1946.

This book is the condensation of a long-continued interest in the problems revolving around men, women and sex. The author has studied the subject extensively and has talked with many persons of all ages and both sexes about problems in this field. His approach is realistic without the sacrifice of good taste. The book is a frank, complete, candid and idealistic discussion of marriage in the broad sense, dealing not only with sex but with economics, sociology and philosophy in their relation to the married state. He discusses at length the choice of a mate. He deals with wartime dislocations, war marriages and the return of soldiers from war, with the hazards to marriage which are a part of the aftermath of war. Any one who has the courage to face facts will find this book a refreshing source of information, advice and inspiration. All young people should read it before marriage rather than after.

Manual of Nursing Procedures, The Mount Sinai Hospital, New York City. Prepared by the Faculty of the Mount Sinai Hospital School of Nursing, Grace A. Warman, R.N., M.A., Principal. Editorial Committee: Blanche D Gubersky, R.N., B.S., Bessie I. Wolfson, R.N., M.A., Felixa B. Sulesky R.N., B.S., and Sylvia T. Farker, R.N. Loose-leaf. Fabrikoid. Price, $3. Pp. 313, with 31 illustrations. Mount Sinai Hospital Press, Fifth Ave. & 100th St., New York 29, 1946.

This compact volume designed to act as a handbook of nursing procedures for nurses in training at the Mount Sinai Hospital, New York, should admirably fulfil that function. It is well organized and well indexed, and the procedures are grouped according to a functional classification which makes reference to a particular procedure relatively easy. Twenty-one drawings give considerable assistance to the text in explaining such procedures as the disinfection of a stool or the setting up of a Wangensteen suction apparatus. Though the descriptions of the nursing procedures are brief, they appear to be adequate. General nursing procedures are covered under the headings of administrative routines, the central supply department, general nursing care, procedures for diagnostic tests and the administration of medicines. Special nursing procedures are included under the titles of medical procedures, procedures for the care of children, surgical procedures, procedures of the specialty services (including otology, ophthalmology, rhinolaryngology and neurology) and nursing care of the orthopedic patient. Operating room procedures and obstetric procedures have not been included in this volume, though a later volume on the former is in preparation. Among the newer procedures described are the intramuscular administration of penicillin, the management of the Wangensteen suction apparatus and the supervision of continuous intravenous infusions and of continuous bladder irrigation apparatus. Among the most valuable inclusions in the appendix are the tables of equivalents, abbreviations, symbols and synonyms.

To those interested in the development of the teaching functions of the nurse it is encouraging to find in Grace A. Warman's foreword the statement that "a knowledge of the patients' social conditions, methods of disease prevention, and the teaching elements of nursing which are included in the present day curriculum help the nurse to take her place in the community as a leader and teacher of health." It is even more encouraging to find the first statement under the method of procedure for treatment of pediculosis in children "Explain the procedure to the patient."

It is to be hoped that this manual will find a well deserved field of usefulness considerably beyond that of the Mount Sinai Hospital School of Nursing.

The Control of Venereal Disease. By R. A. Vonderlehr, M.D., Director, District No. 6, U. S. Public Health Service, and J. R. Heller Jr., M.D., Chief, Venereal Disease Division, U. S. Public Health Service. Foreword by Thomas Parran, M.D., Surgeon General, U. S. Public Health Service. Cloth. Price, $2.75. Pp. 246. Reynal & Hitchcock, 8 West 40th St., New York 18, 1946.

This book is by two doctors, one of whom has been and the other now is chief of the venereal disease division of the U. S. Public Health Service. Through cooperative relationships with state boards of health and secondarily with the larger local health units it has acquired perhaps the most extensive experience outside the armed forces with the venereal disease problem. Even in the armed services the venereal disease problem could be met only with the cooperation of the U. S. Public Health Service.

This book tells how the fight against venereal diseases was brought into the open by shattering the conspiracy of silence

which rendered syphilis and gonorrhea unacceptable words on the radio and made discussion of these diseases taboo except in medical circles. The history of syphilis and its cause are discussed and so are the causes of gonorrhea and the so-called minor venereal diseases. A discussion of treatment is included under the title "Doctors Know How to Win." There are chapters on the use of penicillin, case finding, prostitution, rapid treatment, the relationship of venereal diseases to delinquency and vice versa, the influence of the war and present day control measures. Attention is given to a few typical cases indicating psychologic maladjustments as causes for sexual promiscuity and consequent venereal infections.

The book is written primarily for laymen and can be recommended to them for study. Physicians should read it primarily to familiarize themselves with the procedures advocated by public health authorities and the reasons for the recommendations. It is hardly likely that venereal diseases will be controlled by anything less than complete and well coordinated cooperation between doctors, health officials, sociologists, courts, police and the people at large. This book points the way to such cooperation.

Public Health Nursing in Syphilis and Gonorrhea. By Evangeline Hall Morris, Associate Professor of Nursing, Simmons College, Boston. Cloth. Price, $2.25. Pp. 239, with 18 illustrations. W. B. Saunders Company, W. Washington Square, Philadelphia, 1946.

A book written by a nurse for nurses to further education of nurses in venereal disease has long been needed. Miss Morris has produced that book. The first chapters are devoted to a presentation of the medical aspects of the venereal diseases. The chapter entitled "The Patient and His Needs" will be helpful in considering problems with which many patients are faced and will focus the attention of public health nurses on the patients' needs rather than on the disease alone. The suggested methods of epidemiology do not differ materially from what has already been proposed by many writers but bear repetition, since this phase of the venereal disease program is vital in bringing infectious venereal disease to medical attention. The section on clinic services points out the responsibilities of those staffing venereal disease clinics in making the clinic a desirable place for patients to come. Every nurse could profitably study the excerpts from interviews with two different patients. The inclusion of a chapter on family life education is pertinent, because nurses have many opportunities to guide parents, teachers and other groups in helping children toward attaining a wholesome concept of family life and character development. The author concludes the book with a discussion of the functions and preparation of public health nurses in venereal disease and points out opportunities for effective participation.

Toward Mental Health. By George Thorman. Public Affairs Pamphlet No. 120. Paper. Price, 10 cents. Pp. 32, with illustrations. Public Affairs Committee, Inc., 22 E. 38th St., New York 16, 1946.

This pamphlet is a condensed treatment of the mental hygiene problem in the United States during wartimes and after. It deals with fears, psychosomatic symptoms, war neuroses, moods, retreat from reality and such everyday manifestations of mental illness. It touches also on the organic psychoses and on behavior problems in children. It closes with a statement of the need for a national mental health program. It recognizes the National Committee for Mental Hygiene and the National Mental Health Foundation as organizations working toward better mental health. Like many of the Public Affairs pamphlets which deal factually with scientific and social problems and do not venture in the realm of political remedies for medicosocial illness, this is a useful publication which can be recommended by physicians to their patients interested in mental health problems.

The Challenge of Polio: The Crusade Against Infantile Paralysis. By Roland H. Berg. Introduction by Basil O'Connor, President, The National Foundation for Infantile Paralysis, Inc. Cloth. Price, $2.50. Pp. 208. The Dial Press, Inc., 461 Fourth Ave., New York 16, 1946.

This book is issued by the National Foundation for Infantile Paralysis, Inc., and deals, as its subtitle indicates, with the crusade against infantile paralysis. It is dedicated to the late president Franklin Delano Roosevelt, whose name has been so skilfully used to attract attention to the disease from which he suffered. The book is written for laymen with an introduction by Basil O'Connor, president of the National Foundation for Infantile Paralysis. It begins with a historical review of how poliomyelitis hit the headlines and it outlines Mr. Roosevelt's experiences. Research activities and the failure of various hopeful lines of investigation are reviewed. The alum spray fiasco is described. Experience with vaccines is reviewed, and the situation with respect to the Kenny technic and the associated controversy is reviewed. The book is a worth while historical document and a useful current review, particularly for those lay persons who are asked to work on behalf of the drive for polio foundations and for those who are requested to contribute.

The Popular Medical Encyclopedia: The Standard Guide on Health and Disease. By Morris Fishbein, M.D., Editor, Journal of the American Medical Association and Hygeia, the Health Magazine. Cloth. Price, $4.95. Pp. 540, with illustrations. Doubleday & Company, Inc., Garden City, New York, 1946.

This medical encyclopedia is exactly what its title indicates. It is a popular encyclopedia of medical terms from *abdomen* to *zyme*—the latter short for enzyme or ferment. The articles are short, clearly written and informative. It is not a health book or a textbook. It is exactly what its name indicates, that is, a popular encyclopedia. It should be useful in elementary and secondary schools as a student reference book and in teacher training colleges. It deserves a place in the library of the home where there is interest in matters pertaining to health and medicine.

Die interstitielle Nephritis. Von Privatdozent Dr. H. U. Zollinger, Prosektor am Pathologischen Institut der Universität Zürich. Mit einem Vorwort von Prof. Dr. H. v. Meyenburg. Paper. Price, 28 Swiss francs. Pp. 264, with 87 illustrations. New York & Basel: S. Karger, 1945.

The author's purpose is to review for the pathologist the changes which occur in renal interstitial tissue and to supplement this with personal observations and experiments. His thesis is that many of the interstitial reactions of the kidney are due to the deposition in renal lymphatics of abnormal proteins. The illustrations lack clarity. The specialist in renal pathology may find the volume useful for its bibliography. However, the value of a presentation so specialized that it neglects extrarenal pathologic conditions and only glances cursorily at the concurrent parenchymal changes is almost as scanty as its interest to the clinician.

Sex Problems of the Returned Veteran. By Howard Kitching, M.D. Foreword by Ernest R. Groves, Professor of Sociology, University of North Carolina, Chapel Hill, North Carolina. Cloth. Price, $1.50. Pp. 124 New York: Emerson Books, Inc., 1946.

This book is designed to give the veteran some insight into his problems of integration back into normal family life. It is published a year late to be of much help to the large majority of veterans. The general information contained on the subject of sex and marriage seem more applicable to the young and immature individual who is in need of premarital advice than to the returning veteran. The portion of the book dealing with anxiety as it is related to continence, masturbation and extramarital relationships will probably be the most helpful section to the returning veteran who is willing to wade through some of the rather obvious sociophilosophical discussion.

Estudio crítico del tratamiento médico de la insuficiencia cardíaca. Por Blas Moia, doctor en medicina, docente libre de patología médica de la Facultad de medicina de Buenos Aires. Paper. Pp. 107, with 16 illustrations. "El Ateneo," Florida 340, Cordoba 2099, Buenos Aires, 1945.

In this monograph Moia summarizes the indications for and the mode of action of the several forms of therapy in heart failure as he and others in Buenos Aires practice. Included is a brief description of the physiology of heart failure, the use of digitalis and the other regimens which may be employed, among which are diuretics, bleeding, cupping, purgatives, rest, sedatives and opiates, hypertonic glucose and oxygen. The cardiologist who wishes to be brought up to date on the point of view of the Argentine school will find this manuscript useful. It is well documented and has an extensive bibliography.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

INHERITANCE OF PROGRESSIVE MUSCULAR DYSTROPHY

To the Editor:—A woman aged 29 has three adult brothers with progressive muscular dystrophy and has lost one brother with the same disease. There is no history of this condition in her ancestry. She is seeking advice as to whether she would be liable to transmit this condition if she were to marry and have children.

M.D., Ohio.

ANSWER.—The absence of progressive muscular dystrophy in the immediate ancestry is not unusual, and many cases of this type have been reported in the medical literature. When the observations extend back into the third or fourth generation prior to the appearance of the disease, other cases are frequently disclosed. The appearance of the disease in a single generation is presumptive evidence that progressive muscular dystrophy is propagated by a sex-linked recessive factor. Transmission is effected usually by the females, who do not have clinical signs of the disease, to the males. It would be of value to know the type of progressive muscular dystrophy exhibited in the three brothers of this patient, as there is some variation in the ability to transmit the disease depending on the presenting syndrome.

The means of heredity in progressive muscular dystrophy is not fully known. In the ordinary case, the sex chromosome carrying the dystrophy factor is transmitted by the females of the family for a number of generations. In other instances there may be multiple recessive factors in which the number of factors necessary to induce the condition are fewer for males than for females. Attempts to elucidate the inheritance of muscular dystrophy illustrates the difficulties involved in the application of genetic principles to human problems. The disease probably is inherited in a number of ways. In some families there is transmission by a mendelian dominant; in others by a recessive factor.

The query cannot therefore be answered in a categoric manner. Without more complete knowledge of the appearance of the disease in previous generations, the type of inheritance is not clear. What evidence is available points to the disease in the males only, with probable transmission through the females. The patient would probably have affected male children and non-affected female children, the females acting as carriers for succeeding generations.

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HISTAMINE FOR ARTHRITIS

To the Editor:—Please discuss the use of histamine in rheumatic conditions.

M.D., Mississippi.

ANSWER.—Deutsch was the first to use histamine by iontophoresis for the treatment of arthritis. Most reports in the literature refer to the use of histamine by this method. Definite relief of pain and improvement in motion of joints has been observed. Similar clinical results have been reported following the use of histamine ointment, Imadyl (marketed by Hoffmann-LaRoche). According to reports in the literature this product contains 1 per cent of histamine and information supplied by the manufacturer indicates that it is in the form of the dihydrochloride. Apparently the good results which have been observed are due to the vasodilating effects of the drug.

In man histamine dilates the arterioles, venules and capillaries, irrespective of the manner of administration. It can be given slowly in a 1:250,000 dilution by the drip method and is a safe procedure. It may be used to alleviate acute attacks of allergic or palindromic arthritis. Its value in the treatment of rheumatic conditions is not definitely established, although it does seem to give symptomatic relief in many subjects. More work is necessary before definite conclusions can be drawn regarding its therapeutic value.

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INFECTIOUS RELAPSE AFTER PENICILLIN TREATMENT OF RECENTLY ACQUIRED SYPHILIS

To the Editor:—A man received antisyphilitic treatment with penicillin while in the army in May 1945. In March 1946 he transmitted the disease to his wife. He denies the possibility of reinfection. Have cases of infectious relapse been reported after penicillin treatment of recently acquired syphilis?

F. C. Katzenstein, M.D., Salem, Ill.

ANSWER.—Infectious relapse is a finding of all investigators studying the penicillin therapy of syphilis when the drug employed in the treatment of a recently acquired infection is insufficient to arrest the disease. Using total dosages of 1.2 million Oxford units of sodium penicillin, the amount of drug employed in most published material to date, the incidence of infectious relapse reported by various authors is from 1 to 5 per cent. Actually more recent experience has indicated that it is probably considerably in excess of these figures.

The first detectable relapsing lesion will usually occur from four to six months after therapy has been completed, though lesions are known to have resulted within the first month and after more than one year. Whenever treatment fails to cure freshly acquired syphilis, infectious relapse and transmission of the disease under favorable circumstances are accordingly a possibility. Pillsbury's report from the European theater of operation (*Am. J. Syph., Gonor. & Ven. Dis.* **30:**134 [March] 1946) indicates that soldiers treated there with penicillin for syphilis yielded a known incidence of infectious relapse of 1 to 2 per cent, and statistical data are given on 72 such cases. There is a distinct possibility that soldiers under such circumstances returning to civilian life will infect their marital partner unless medical supervision continues to be adequate during the transition period from military to civilian life.

Failure of serologic response or serologic relapse is often a premonitory sign of impending infectious relapse and warns of the development of clinically demonstrable lesions containing Treponema pallidum. Thus, most patients who fail to respond to penicillin therapy will maintain a high serologic titer for syphilis when a quantitative test is employed or will show an increasing titer following the initial reduction. The test will at times, of course, become completely negative only to revert to positive when infectious lesions develop, or shortly before.

Medical follow-up of all penicillin treated cases of early syphilis should consist of a blood serologic test and physical inspection for skin and mucous membrane lesions on approximately a monthly basis for at least the period during which relapse is likely to occur. That would be, according to our present knowledge, for a minimum of ten to twelve months after the completion of therapy. Among the most important facts which determine the possibility of relapse are total dosage of penicillin employed and the duration of the disease when treatment is commenced. Thus in the initial publications of penicillin therapy of early syphilis (J. E. Moore and others, THE JOURNAL, Sept. 9, 1944, p. 67) the percentage of serologic and clinical relapse combined was 3.2 for seronegative primary, 5 for seropositive primary and 10 for early secondary syphilis. This same study mentions 31 cases of clinical relapse in early syphilis following penicillin therapy. Small dosage of penicillin is particularly prone to result in infectious relapsing syphilis, as is shown in the experimental study by G. W. Binkley and his associates (Rapid Treatment of Early Syphilis with Small Doses of Penicillin, *Arch. Dermat. & Syph.* **51:**200 [March] 1945) and in the increasing number of reports of development of infectious syphilis following the use of penicillin to treat some other dis-

ease, in particular gonorrhea (Atcheson, D. W.: Secondary Syphilis Following Penicillin Therapy of Gonorrhea, *Am. J. Syph., Gonor. & Ven. Dis.* **29**:423 [July] 1945. Walker, A. E., and Barton R. L.: The Treatment of Gonorrhea with Penicillin During the Incubation Period of Early Phase of Syphilis, *Ven. Dis. Inform.* **26**:241 [Nov.] 1945. Leifer, William, and Martin, S. P.: Penicillin in Early Syphilis, THE JOURNAL, Jan. 26, 1946, p. 202. Fromer, S.; Cutler, J. C., and Levitan, S.: Masking Early Syphilis by Penicillin Treatment of Gonorrhea, *Ven. Dis. Inform.* **27**:174 [July] 1946).

POSSIBLE MASCULINIZING TUMOR

To the Editor:—A woman aged 22, a primipara, sixteen months post partum developed a husky, gruff, somewhat hoarse, male type of voice, about the third or fourth month of pregnancy. Competent study of the nose and throat fails to reveal any underlying cause. Complete physical examination does not show any male type secondary sex characteristics or any other abnormality. Please discuss the diagnosis and treatment.

M.D., New York.

ANSWER.—The main problem in a patient like this is whether or not there is a masculinizing tumor in either the adrenal cortex or an ovary. A careful search should be made for other masculinizing changes, such as growth of hair on the face, chest, abdomen, arms and legs, enlargement of the clitoris, decrease in the size of the breasts and long periods of amenorrhea. An abdominal and pelvic examination should be carried out. Often a tumor can be felt on physical examination alone. If a tumor is not felt, a flat plate should be made of the genitourinary tract. If this is negative, an intravenous pyelogram might be of some value in demonstrating a tumor of the adrenal cortex. It would also be of some value to determine the amount of 17-ketosteroids in the urine. In masculinizing tumors the concentration is usually greatly increased, sometimes tenfold. If all findings are negative and the only change is in the voice, the patient may be followed closely without resorting to surgical intervention. If, however, a definite tumor is found or if there are chemical changes in the urine that point to one, both the ovaries and adrenals should be explored surgically.

MISSED ABORTION

To the Editor:—Please discuss the following case: A woman aged 44, married, of Norwegian birth, with an entirely negative menstrual and other past history, had her last period which was normal, Feb. 22-27, 1946. Without other signs of pregnancy, small amounts of bright blood from the uterus appeared on April 29 and continued daily for one week. The patient was then hospitalized. All laboratory findings were negative except a positive Aschheim-Zondek test. The lower part of the abdomen was filled with a firm tumor of regular outline, evidently the uterus, with the consistency of a fibroid rather than a pregnancy. The clinical impression was early pregnancy and intramural fibroid, with impending spontaneous abortion. With bed rest the patient's general condition has remained unchanged but the tumor has steadily decreased to less than one third of its former size and has become softer. A negligible amout of blood has been lost in the past three weeks. At times a small amount of brownish material has been noted, which on one occasion had an offensive odor. There has been no bleeding or discharge for the past five days. The tumor apparently is still regressing in size. Roentgenograms do not reveal fetal parts.

M.D., Massachusetts.

ANSWER.—This is almost certainly a case of missed abortion. Another Aschheim-Zondek test should be performed and will almost certainly be negative unless there is still some living chorionic ectoderm in the uterus. Regardless of the result of the biologic test, a curettement should be performed to remove the remains of the pregnancy. It is possible that nature has already expelled the entire ovum or will soon do so. Therefore one may wait to see if the uterus will stop diminishing in size and normal menstruation will return. If the menses do not return in two months and a new gestation has not begun, and certainly if bleeding is profuse or irregular, a curettage should be done. X-ray films will rarely reveal fetal parts before four months of development, so the absence of fetal parts has no significance in this case.

CLINICAL PATHOLOGY

To the Editor:—What is the definition of "clinical pathology?" How and where did the term originate? Please give references.

Kano Ikeda, M.D., St. Paul.

ANSWER.—The constitution and by-laws of the American Society of Clinical Pathologists defines clinical pathology as "that branch of the science and practice of medicine which consists of the application of pathologic anatomy, physiology, chemistry, parasitology and bacteriology to the diagnosis of disease."

This comprehensive definition, adopted in 1934, expresses a growth which began centuries ago with the examination of urine and which blossomed out in the first half of the nineteenth century in the application of microscopy and chemistry to clinical medicine and in the second half of the same century in the application of bacteriology and more recently in the application of immunology.

The exact origin of the term "clinical pathology" is difficult to establish. One finds it as early as 1865 in the name of The Clinico-Pathological Society of Washington, D. C. Its proceedings were published in the *Journal of Medical Sciences* **55**: 120-128, 412-418, 1868. These are clinical case reports with occasional necropsy findings and urinalyses.

W. Essex Wynter and Frank J. Wethered are the authors of "A Manual of Clinical and Practical Pathology" published in 1890 by Blakiston. The introduction is of historical interest. It states as the object of the book "to embrace . . . a description of various methods which may be employed in the investigation of morbid changes both before and after death. For the most part chemistry, pathology and clinical medicine have hitherto been studied separately, whereas in many of their aspects they are so mutually involved that it is absolutely necessary to consider them together."

Clinical pathology appears as a subheading of pathology for the first time in 1905 in volume XII of the second series of the Index Catalogue of the Library of the Surgeon General's Office. There one finds on page 666 a series of papers published between 1904 and 1907.

LUPUS ERYTHEMATOSUS

To the Editor:—What is the latest treatment of lupus erythematosus? Allergy has been reported as a possible cause of lupus erythematosus. Is Benadryl of any value as reported by a "lay" publication?

E. J. Wintenburg, M.D., Van Nuys, Calif.

ANSWER.—There is no valid reason for the belief expressed recently by Teilum (*Acta med. Scandinav.* **123**:126, 1946) that disseminated lupus erythematosus is related to allergy. Unlike periarteritis nodosa, lupus erythematosus is not associated with a clinical history or manifestations of allergy such as urticaria, eczema, asthma or eosinophilia. It is true that the fibrinoid degeneration of connective tissue characteristic of advanced lupus erythematosus, which is responsible for the changes in the walls of small blood vessels and in serous membranes, is also seen in allergic diseases and can be reproduced in experimental animals by the injection of bacterial and other foreign proteins (Rich, A. R., and Gregory, J. E.: *Bull. Johns Hopkins Hosp.* **72**:65 [Feb.], **73**:239 [Oct.] 1943). But this connective tissue change is not specific for allergy, for it can be found in a variety of nonallergic conditions associated with connective tissue injury—around foreign bodies, in the base of a peptic ulcer, in diffuse scleroderma, in chronic infections.

Benadryl has been used in the treatment of lupus erythematosus but has not been found to be of value. There is as yet no specific therapy for the disease. The patient's nutrition should be improved by a well balanced diet, high in calories and reinforced with supplementary vitamins. Protection against bright light sometimes seems to be of value. Intercurrent infections should be promptly controlled with the appropriate antibiotic. In a few instances remissions have been associated with the administration of testosterone propionate or with castration, but the causal relationship is not convincing. This form of therapy has been based entirely on the fact that 95 per cent of the cases of disseminated lupus erythematosus occur in females.

DIET AND MEDICATION AFTER CHOLECYSTECTOMY

To the Editor:—Please discuss diet and medication following cholecystectomy.

M.D., New York.

ANSWER.—A special diet is not usually required by patients following a cholecystectomy. While the storage function of the gallbladder is lost, no disturbance in the absorption and digestion of fat or other foodstuffs results from this fact. For a time at least following the operation there occurs a more or less continuous flow of bile into the duodenum. In the normal person the bile secreted in the intervals between meals is stored in the gallbladder, where it undergoes concentration. Evacuation of the gallbladder occurs when food from the stomach enters the duodenum. Theoretically this should make for the better digestion and absorption of fat in the intestine. The factor of safety is so great, however, that no discoverable disturbance in digestion occurs when the flow of bile into the intestine is continuous rather than intermittent. As time goes on the common bile duct becomes dilated following cholecystectomy and an intermittent flow of bile into the intestine becomes partially reestablished.

USE OF FLUIDS IN CRANIOCEREBRAL INJURIES

To the Editor:—Since the surplus army and navy dried plasma became freely available for civilian medical practice in abundant supply, I have noted many instances in which this plasma is being used for patients with fractured skulls without outward signs of shock and not being prepared for any immediate operative procedure. Apparently the rationale of this therapy is to prevent shock and to maintain the osmotic pressure of the blood and possibly reduce intracranial pressure. The plasma is being given in fairly large amounts, varying from 250 to 1,000 cc., reconstituted to its original volume. The question arises as to whether the use of these large amounts of isotonic plasma may not be more harmful than beneficial, because of the possibility of the increased blood volume causing an increase in intracanial pressure. I would appreciate a discussion of the use of intravenous fluids in the presence of a fractured skull, with particular emphasis on the use of hypertonic preparations such as concentrated albumin, glucose or magnesium sulfate preparations.

M.D., New York.

ANSWER.—There are few subjects in medicine that have been characterized by as much loose thinking, talking, writing and practice as has the use of fluids in cases of craniocerebral injury. In this connection there are certain facts which must not be lost sight of. First and foremost, the victims of craniocerebral injuries are as much in need of fluids and a proper fluid, electrolyte and protein balance as is any other type of patient. Second, it is impossible to dehydrate the brain without at the same time dehydrating the patient as a whole. Third, cerebral edema plays only a relatively small role in the picture of craniocerebral injury. Dehydration and the use of hypertonic solutions of any kind have little place in the treatment of such injuries. Without doubt the use of such solutions and dehydration has resulted in far more damage than they have good. Certainly one can produce shrinkage of the brain by the use of hypertonic solutions intravenously; but, unless a serious state of dehydration is maintained thereafter, the shrinkage of the brain will not persist. The use of hypertonic solutions in cases of craniocerebral injury should be limited to those relatively few instances in which it becomes necessary to reduce intracranial tension temporarily while preparing to provide more permanent relief surgically.

It is now generally recognized that the only adequate treatment for shock is whole blood given intravenously promptly and in sufficiently large quantities to supply the patient's needs whatever they may be. Plasma and serum are not satisfactory substitutes for whole blood. Their use in such circumstances is excusable only until whole blood can be secured. On the other hand, plasma may be preferable when one seeks to repair a protein deficiency. This would rarely be desirable for a patient with a recent craniocerebral injury. The use of 250 to 1,000 cc. of fluid, be it plasma or other isotonic fluid, would rarely be harmful to a patient with such an injury. In fact it frequently would be desirable as a means of insuring that the patient had adequate fluids. However, as noted previously, there would only rarely be instances in which plasma would be the fluid of choice.

PAINFUL UTERINE CONTRACTIONS DURING PREGNANCY

To the Editor:—A secundipara, tertigravida, complains of contractions of the uterus which are not painful but have been troublesome during the last four and one-half months of the pregnancy. When they occur they temporarily incapacitate her and they become more frequent and severe as the pregnancy progresses. The first labor was associated at its onset with spontaneous rupture of the membranes just before term but was otherwise normal. During the second pregnancy contractions began at four and one-half months, and various antispasmodics and sedatives were used, with negligible results. Labor was one month premature, with spontaneous rupture of the membranes four days prior to delivery. The contractions during the last two months of that second pregnancy were so severe as to incapacitate her for even the lightest tasks. Is this condition physiologic? Should continued sedation be used or is there any specific preparation for the condition?

Louis H. Bos, M.D., Chicago.

ANSWER.—The uterus is a hollow muscular organ which exhibits spontaneous contractions particularly during pregnancy. These become progressively more frequent and stronger as term is approached, eventuating in labor. Painful uterine contractions may occur at any time during pregnancy, but they are most common in the last few months. They resemble labor pains, with the exception that they vary in duration, intensity and frequency and follow no rhythmic pattern. Late in pregnancy they constitute the premonitory phase of labor and probably are responsible for much of the effacement of the cervix.

There is no specific therapy for the relief of these painful uterine contractions. Sedatives such as the barbiturates are used most commonly, but although they rarely stop the contractions they allow the patient to obtain much needed rest. Rest is helpful, for activity increases their severity. Calcium, orally and intravenously, has been used with varying results. More recently magnesium has been suggested. Endocrine substances, particularly progestin, has been recommended, but the results are not striking.

POSSIBLE TOXICITY OF PHENYL-MERCURIC BORATE USED AS PRESERVATIVE FOR PLASMA

To the Editor:—What is the toxicity of phenyl-mercuric borate used as a preservative for dried plasma? Is there any danger if plasma containing it is administered in large quantities (5 to 10 units of 250 cc. each within a period of twenty-four to forty-eight hours) to patients with such illnesses as burns covering a large surface of the body area? This plasma contains sufficient phenyl-mercuric borate to constitute a 1:50,000 dilution when the plasma is restored for use.

M.D., New York.

ANSWER.—Phenyl-mercuric borate combines with plasma proteins so that its toxicity is changed and probably lowered. When a patient receives large doses of plasma containing a 1:50,000 dilution of phenyl-mercuric borate, for instance 10 units of 250 cc. each, he receives 50 mg. of phenyl-mercuric borate. With such an amount, especially in the case of burns with already damaged kidneys, the possibility of toxic action cannot be overlooked.

It is not necessary to add preservatives to plasma to preserve in the dried or frozen state. With ordinary precautions the stability can be safely maintained without the addition of preservatives. When large doses of plasma are used (over 2,000 cc. in twenty-four hours), preference should be given to plasma containing no preservatives. For smaller doses such precaution is not needed.

PREMENSTRUAL BLEEDING

To the Editor:—A common complaint in my practice is a brownish vaginal discharge for from three to nine days prior to the onset of the menses. Most of the patients are young, healthy and apparently normal women. Please discuss this problem and the treatment indicated.

M.D., Michigan.

ANSWER.—The brown discharge is mild premenstrual bleeding and is not uncommon. It is usually due to the hyperemia which is present in all the pelvic organs, but in most instances an abnormality of the cervix will be found such as so-called erosions or polyps. Hence in all cases of premenstrual brown or bloody discharge a complete pelvic examination should be made, including the use of a vaginal speculum. Removal of cervical polyps and cauterization of erosions will cure most of the cases.

TREATMENT OF CEREBRAL HEMORRHAGE

To the Editor:—Prior to my entering the service I had a patient who developed a paralysis of the vocal cords and the entire right side of his body after a cerebral hemorrhage. On my return he is still unable to talk but can use his leg and arm to some extent. His son, who is still in the service, feels that something can be done for his father in the way of brain surgery. Is there any one in this country who could relieve this man by surgery?

M.D., Iowa.

ANSWER.—It would be impossible to give a satisfactory answer to this query without having available a detailed history of the development and course of the patient's disability and the results of a careful neurologic and general physical examination, plus such laboratory data as might then appear indicated. If the original diagnosis of "cerebral hemorrhage" is correct, or if the patient suffers some other type of cerebrovascular disorder such as a cerebral thrombosis, there is nothing that neurologic surgery would have to offer. There are numerous competent neurologic surgeons throughout the United States to whom this patient could be referred for an examination and an opinion as to the possibilities of surgical treatment. Those who have been certified are so indicated in the American Medical Directory or are listed in the Directory of Medical Specialists.

KELOID; HERNIA OF ANTERIOR TIBIAL MUSCLE

To the Editor:—In The Journal of Sept. 21, 1946 a doctor from Pennsylvania asks what he can do to remove a keloid scar. The multiplicity of suggestions does not seem to be very helpful. Postoperative patients with hyperthyroidism consistently have fine hairline scars, but sufficient attention has not been paid to this fact. I suggest that the doctor carry the patient up to a tolerance dosage of thyroid for about three weeks and then surgically excise the scar and continue the thyroid for six to eight weeks after the operative removal. I think he will be well pleased with the result. In the same issue the statement is made that it is relatively easy to close fascial defects producing hernias of the anterior tibial muscle. I agree that the hernias which do not produce symptoms do not need treatment. However, it is not relatively easy to close these fascial defects, particularly in cases associated with symptoms, and the closure of such defects does not consistently produce relief of the symptoms. A much easier and more successful procedure is to make a small incision and split the sheath subcutaneously so that the opening is large instead of small. It is not necessary to make a long incision, as it can be done subfacially with scissors.

Duncan C. McKeever, M.D., Houston, Texas.